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GRANT NUMBER DAMD17-94-J-4437

TITLE: Cancer Prevention and Control Research Manpower  
Development

PRINCIPAL INVESTIGATOR: Samuel J. Shacks, Ph.D., M.D.

CONTRACTING ORGANIZATION: Charles R. Drew University of  
Medicine & Science  
Los Angeles, CA 90061

REPORT DATE: October 1996

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<b>13. ABSTRACT (Maximum 200)</b>  The primary aim of this project in year two was to complete the recruitment of six post-doctoral graduates. Sherry Crump, MD, MPH, Mosunmola George-Taylor, MS, Anthony Highshaw, MD, Vanessa Parker, Ph.D., Ling Wu, Ph.D. and Kangman Zhu, MD, Ph.D. were recruited. Dr. Crump is being mentored by Beverly Taylor, MD at Morehouse School of Medicine. Dr. George-Taylor is being mentored by Linda Pederson, Ph.D. of Morehouse School of Medicine. Dr. Parker is working with Patricia Matthews-Juarez, Ph.D. and Samuel Shacks, Ph.D., MD at Drew University. Dr. Wu is working with Kofi Semenya, Ph.D. of Meharry Medical College. Dr. Zhu is being mentored by Robert Levine, MD of Meharry Medical College. Curriculum vitae's of fellows and their mentors are in appendix A.  The fellows have made excellent progress during year two. Dr. Zhu received funding for two grants and prepared three articles. Two have been accepted for publication in peer reviewed journals. Dr. Crump submitted a proposal for extramural funding and is preparing an article for publication. Dr. George-Taylor is working on a research project about electromagnetic exposure and breast cancer. Dr. Parker submitted a proposal for extramural funding and is preparing several articles for publication. Dr. Wu is developing a research project on risk factors of breast cancer. Dr. Highshaw resigned his fellowship in order to conduct prostate cancer research project at another institution.				
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## FOREWORD

Opinions, interpretations, conclusions and recommendations are those of the author and are not necessarily endorsed by the U.S. Army.

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\_\_\_ For the protection of human subjects, the investigator(s) adhered to policies of applicable Federal Law 45 CFR 46.

\_\_\_ In conducting research utilizing recombinant DNA technology, the investigator(s) adhered to current guidelines promulgated by the National Institutes of Health.

\_\_\_ In the conduct of research utilizing recombinant DNA, the investigator(s) adhered to the NIH Guidelines for Research Involving Recombinant DNA Molecules.

\_\_\_ In the conduct of research involving hazardous organisms, the investigator(s) adhered to the CDC-NIH Guide for Biosafety in Microbiological and Biomedical Laboratories.

*Samuel Sharkey* 10/28/96  
\_\_\_\_\_  
PI - Signature Date

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## **Introduction**

Breast cancer is a leading cause of death in American women. Women of minority groups have higher mortality rates for this disease compared to white women. To address this issue, efforts to increase minority representation in cancer research have been made by the National Institute of Medicine. Success of these activities have been limited, and the pool of minority investigators remains small. The purpose of this project is to expand the pool of minority cancer control and prevention investigators. The overall aim of this three year study is to provide training in breast cancer prevention and control research for six post-doctoral graduates. The ultimate goal is to create independent investigators who will obtain extramural funding upon completion of the fellowship. The hypotheses to be tested is that with "protected time" and appropriate mentors doctoral graduates in social science and public health disciplines can achieve independent extramural funding for breast cancer research within three years. Fellows are paired with faculty mentors from one of three Cancer Centers; Drew University of Medicine and Science in Los Angeles, California, Meharry Medical College in Nashville Tennessee and Morehouse School of Medicine in Atlanta Georgia.

## **Body**

The primary aim of year two of the study was to complete the recruitment of six post-doctoral graduates. During year one of the study, two fellows were recruited. Four additional fellows were recruited in year two. A description of each fellow's progress toward independent funding is summarized below.

Sherry Crump, M.D., M.P.H. is a preventive medicine physician who is being mentored by Beverly Taylor, MD, MPH at Morehouse School of Medicine. To date, Dr. Crump has completed two years of the fellowship. During year two of the grant, Dr. Crump finished her study "Barriers to Screening Mammography Utilization Among Black Women at Grady Memorial Hospital" (See appendix B1 for detailed description of her project). Based on the results of this study, Dr. Crump designed interventions to improve screening mammography compliance rates at Grady hospital in Atlanta. Proposals to fund these interventions have been sent to the U.S. Army Department of Defense's Breast Cancer Research Program and to the Grady Memorial Hospital Indigent Care Trust Fund. Award notification from both sources are pending. Dr. Crump presented her results to several different organizations (See Appendix B2 for a list of these presentations). During next year, Dr. Crump plans to publish an article, and she, also, intends to present her results at the American Public Health Association Meeting on November 19, 1996. (See Appendix B3 for work schedule).

Mosunmola George-Taylor, Ph.D. is a cell biologist. She began the fellowship in June 1996. Linda Pederson Ph.D. at Morehouse School of Medicine serves as her mentor. Dr. George-Taylor has developed a research project, "Electromagnetic Field Exposure and The Occurrence of Breast Cancer in Women" (See Appendix C for study methodology). She is preparing an article for publication and plans to apply for extramural funding soon.

Anthony Highshaw, MD joined the fellowship during year two of the grant and six months later resigned to conduct prostate cancer research at another institution. Efforts are being made to recruit a replacement.

Vanessa Parker, Ph.D. ,preventive health, is a recent graduate of the University of Southern California. She joined the fellowship in December of 1995. She is being mentored by Drs. Matthew-Juarez and Shacks. During this year, Dr. Parker developed and administered a breast health survey

to ethnic minority women attending a community-based breast health screening (See appendix D1). Data analysis will look at ethnic differences for factors influencing women getting clinical breast exams and/or mammogram. She submitted a proposal to the Los Angeles County Breast Cancer Early Detection Program (LAC-BCEDP) on 10/7/96 (See Appendix D2). The purpose of the proposal is to evaluate a breast health education intervention targeting African American female residents of a public housing community. Dr. Parker is currently preparing several grants and publications related to breast cancer control and prevention.

Kangman Zhu, MD, MPH, Ph.D. is an epidemiologist who is mentored by Robert Levine, MD, MPH at Meharry Medical College. Dr. Zhu has completed two years of the fellowship. During year two of the study, Dr. Zhu was awarded over \$700,000 for two research studies from the Department of Defense; "An Intervention Study on Screening for Breast Cancer Among Single African-American women Aged 65 and Older" and "Breast Cancer and Risk Factors Among African-American Women aged 20-54. Dr. Zhu, also, prepared three articles. Two will be published in peer review journals within a few months See Appendix E).

Ling Wu, Ph.D. is the most recent fellow. He is working with Kofi Semanya, Ph.D. at Meharry Medical College. Dr. Wu is developing a research project titled "Risk Factors of Breast Cancer in Older African-American women. He has completed the literature review and is currently collecting data from the state of Tennessee.

All of the fellows, except for Dr. Wu, presented their projects at the annual Consortium Cancer Center Symposium.

### Conclusion

Year two of this grant has been highly successful. Both of our second year fellows, Drs. Crump and Zhu have been very productive. Dr. Zhu has exceeded our desired goal regarding extramural funding in order to become an independent investigator. The prospect of a successful outcome for Dr. Crump is also promising. All of our first year fellows are proceeding at a consistent and accelerated rate. It is anticipated that all of them will become independent researchers in breast cancer control and prevention. This year we experienced the unexpected loss of one fellow. Dr. Highshaw is at another institution conducting research in prostate cancer. Our loss, however, represents an overall contribution to expanding the number of minority investigators in cancer control and prevention. We request an opportunity to fill the remaining position, although we recognize that this fellow will have less than one year of funding. We anticipate that we will be able to recruit successfully.

**APPENDIX A**



**BIOGRAPHICAL SKETCH**

Provide the following information for the key personnel in the order listed on Form Page 2.  
Photocopy this page or follow this format for each person.

NAME Sherry R. Crump, MD, MPH		POSITION TITLE Research Fellow	
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)			
INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY
University of Virginia, Charlottesville, VA	B.A.	1981-85	Biology
University of Virginia, Charlottesville, VA	M.D.	1985-91	Medicine
Carolina's Medical Center, Charlotte, NC		1991-92	Internship-Pediatrics
Morehouse School of Medicine, Atlanta, GA		1992-94	Residency-Prev. Med.
Rollins School of Public Health, Emory, Atlanta	MPH	1992-95	Public Health

RESEARCH AND PROFESSIONAL EXPERIENCE: Concluding with present position, list, in chronological order, previous employment, experience, and honors. Include present membership on any Federal Government public advisory committee. List, in chronological order, the titles, all authors, and complete references to all publications during the past three years and to representative earlier publications pertinent to this application. If the list of publications in the last three years exceeds two pages, select the most pertinent publications. DO NOT EXCEED TWO PAGES.

**PROFESSIONAL EXPERIENCE:**

1987-1988 Project Bayon-Volunteered in a hospital for indigent inhabitants of Honduras, Central America  
 1992-1993 Atlanta Public School for the Special Olympics Program - Volunteer Physician  
 1992-1994 Georgia Nurses' Foundation Health Care for the Homeless Program - Volunteer Program  
 1992-Present Fulton County Health Department Teen Service Program - Staff Physician  
 1994-Present Drew/Meharry/Morehouse Consortium Cancer Center - Breast Cancer Prevention and Control Research Fellowship

**HONORS AND MEMBERSHIPS:**

Summer '92 Treatment and Follow-up Compliance of Atlanta Soviet Refugees - Georgia Department of Human Resources, Office of Rural Health  
 Spring '93 Emory Undergraduate Student Sexual Behavior Survey - Rollins School of Public Health Emory University  
 Fall '93 Domestic Violence Survey - Georgia Department of Human Resources, Division of Public Health, Epidemiology Branch  
 Spring '94 Gonorrhea Trends - Richardson Health Center, STD Clinic, 1990-1993, Dekalb County Board of Health, Georgia

**SELECTED PUBLICATION:**

Crump, S.R. Promotion of Health Eating Habits in Children (letter to the editor) J Pediatric 1995; 126:850-851

**BIOGRAPHICAL SKETCH**

Provide the following information for the key personnel in the order listed on Form Page 2.

Photocopy this page or follow this format for each person.

NAME		POSITION TITLE	
Mosunmola Alaba George-Taylor		Assistant Professor	
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)			
INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY
University of Lagos, Akoka, Lagos, Nigeria	B.S.	1975	Chemistry
Atlanta University, Atlanta, GA	M.S.	1982	Physical Chemistry
Georgia Institute of Technology, Atlanta, GA	M.S.	1987	Atmospheric Chemistry
Clark-Atlanta University, Atlanta, GA	Ph.D.	1994	Biology

RESEARCH AND PROFESSIONAL EXPERIENCE: Concluding with present position, list, in chronological order, previous employment, experience, and honors. Include present membership on any Federal Government public advisory committee. List, in chronological order, the titles, all authors, and complete references to all publications during the past three years and to representative earlier publications pertinent to this application. If the list of publications in the last three years exceeds two pages, select the most pertinent publications. DO NOT EXCEED TWO PAGES.

**PROFESSIONAL EXPERIENCE:**

1990-Present Assistant Professor, Chemistry Department, Clark Atlanta University, Atlanta, GA  
 1991-1994 Research Technician, Department of Biological Sciences, Clark Atlanta University, Atlanta, GA  
 1993-1994 Teaching Assistant, Clark Atlanta University, Atlanta, GA  
 1991-1994 Biology and Chemistry Instructor, Clark Atlanta University summer programs  
 1992-1993 Chemistry Lab Instructor, Spelman College, Atlanta, GA  
 1991-1992 Science Instructor, Clark Atlanta University Weekend Programs Saturday Science Academy  
 1992 Instructor of Hands on Laboratory Procedures in Physical Science  
 Kindergarten through K8 Teachers in Atlanta Public School System.  
 1988-1990 Research Assistant, Dolphus E. Milligan Science Research Institute, Clark Atlanta University  
 Atlanta, GA  
 1989 Laboratory Instructor, Chemistry Department, Clark Atlanta University, Atlanta, GA  
 1982-1988 Research Assistant, School of Geophysical Sciences, Georgia Institute of Technology,  
 Atlanta, GA  
 1980-1982 Research Assistant, Chemistry Department, Atlanta University, Atlanta, GA  
 1977-1980 Chemistry Teacher, Ikeja Grammar School, Oshodi, Lagos State, Nigeria  
 1975-1976 Chemistry Teacher, Lagos City College, Yaba, Lagos State, Nigeria  
 1972 Laboratory Technician, Lagos University Teaching Hospital, Idi-Araba, Lagos State, Nigeria

**HONORS AND MEMBERSHIPS:**

Member of the American Society of Cell Biology (ASCB).  
 Member of the Federation of American Society of Experimental Biology (FASEB)

**PROFESSIONAL CONFERENCES AND ACTIVITIES:**

Drew-Meharry-Morehouse Cancer Consortium Symposium, Nashville, Tennessee, 1995  
American Society of Cell Biologists Conference, San Francisco, California, 1994  
American Society of Cell Biologists Conference, New Orleans, Louisiana, 1993  
American Society of Cell Biologists Conference, Denver, Colorado, 1992  
American Society of Cell Biologists Conference, Boston, Massachusetts, 1991  
American Society of Cell Biologists Conference, San Diego, California, 1990  
National MBRS (Minority Biomedical Research Symposia) Conference Atlanta, Georgia, 1993  
National MBRS Conference, Washington, D.C., 1991  
National MBRS Conference, Nashville, Tennessee, 1990  
American Chemical Society 18th Regional Meeting, Bowling Green, Ohio, 1986

Successfully completed a short course on "Remote Sensing of the Earth and Atmosphere", conducted by the Department of Continuing Education, Georgia Institute of Technology, Atlanta, GA May 13-14, 1985

Successfully completed a short course on the "Introduction of the Problems of Acid Rain", conducted by the Department of Continuing Education, Georgia Institute of Technology, Atlanta, Ga November 7-10, 1984

**SELECTED PUBLICATION:**

Low Temperature Infrared Spectrum of Chlorine Nitrate and Evidence for the Existence of ClOONO. Journal of Physical Chemistry (1983), 87, 1091.

## BIOGRAPHICAL SKETCH

Give the following information for the key personnel and consultants and collaborators. Begin with the principal investigator/program director. Photocopy this page for each person.

NAME	POSITION TITLE
Robert S. Levine	Co-Investigator

EDUCATION (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)

INSTITUTION AND LOCATION	DEGREE	YEAR CONFERRED	FIELD OF STUDY
Columbia University, NY, NY	B.A.	1963	Pre-Med.
Bowman Gray, Winston-Salem, NC	M.D.	1968	Medicine
Bowman Gray, Winston-Salem, NC	Intern	1969	Pediatrics
University of Kentucky, Lexington, KY	Resident	1972	Preventive Medicine

RESEARCH AND PROFESSIONAL EXPERIENCE: Concluding with present position, list, in chronological order, previous employment, experience, and honors. Key personnel include the principal investigator and any other individuals who participate in the scientific development or execution of the project. Key personnel typically will include all individuals with doctoral or other professional degrees, but in some projects will include individuals at the masters or baccalaureate level provided they contribute in a substantive way to the scientific development or execution of the project. Include present membership on any Federal Government public advisory committee. List, in chronological order, the titles, all authors, and complete references to all publications during the past three years and to representative earlier publications pertinent to this application. DO NOT EXCEED TWO PAGES.

## Employment:

1972-74 Preventive Medicine Officer, Fort Hood, TX  
 1974-76 Physician II, Dade Co. Health Dept., Miami, FL  
 1976-86 Asst.-Associate Professor and Vice Chairman, Dept. of Epidemiology and Public Health, University of Miami, School of Medicine, Miami, FL  
 1986-88 Director of Epidemiology and Biostatistics, Nassau Co. Dept. of Health, Mineola, NY  
 1988-91 Director of Community and Preventive Medicine, Our Lady of Mercy Medical Center, Bronx, NY  
 1991 Associate Medical Director, Quality Assurance, Kings Co. Hospital Center, Brooklyn, NY  
 1992-Present Professor, Department of Family and Preventive Medicine, Meharry Medical College, Nashville, TN  
 1993-Present Principal Investigator, MEDTEP Research Center, Associate Director for Research, Institute on Health Care for the Poor and Underserved, Chair, Editorial Board of Journal of Health Care for the Poor and Underserved, Meharry, Medical College, Interim Chair, Department of Family and Preventive Medicine, Meharry Medical College, Nashville, TN

## Honors and Awards:

1972 Army Commendation Medal  
 1975 Fellow, American College of Preventive Medicine  
 1988 Member, American College of Epidemiology

## Publications: (1990-Present)

- Report of a WHO/UNEP Working Group. Public Health Impact of Pesticides Used in Agriculture. Geneva and Nairobi: WHO/UNEP. 1990.
- Zeigler RG, Brinton LA, Warnecke R, Hamman RA, Lehman H, Levine RS, Stolley P, Rosenthal AC, Trumbell AC, Hoover RN. "Diet and the Risk of Invasive Cervical Cancer Among White Women in the United States." Amer J Epidemiol. 132:432-445. 1990.
- Levine RS, Hersh CB, Hodder RA. "Historical Patterns of Pesticide Epidemiology Research." Epidemiology. 1:181-184. 1990.
- Jones CJ, Brinton LA, Hamman RF, Stolley PD, Lehman HF, Levine RS. "Risk Factors for In Situ Cervical Cancer: Results from a Case-control Study." Cancer Research. 50:3657-3662. 1990.
- Hidesheim A, Brinton LA, Mallin K, Lehman HF, Savitz DA, Levine RS. "Barrier and Spermicidal Contraceptive Methods and Risk of Invasive Cervical Cancer." Epidemiology. 1:266-272. 1990.
- 6-8. The Selected Cancers Cooperative Study Group. The Association of selected cancers with service in the US military in Vietnam. I. Non-Hodgkin's Lymphoma; II. Soft Tissue and Other Sarcomas; III. Hodgkin's Disease, Nasal Cancer, and Nasopharyngeal Cancer. Arch. Intern Med. 150:2473-83; 2492-95; 2495-2505. 1990

# Biographical Sketch: Robert S. Levine, M.D. (Page 2)

9. Levine RS. "Recognized and Possible Effects of Pesticides in Humans." Chapter 7 of Hayes WJ Jr., and Walls EN. Handbook of Pesticide Toxicology. Vol. I. San Diego: Academic Press. 1991. pp. 275-360.
10. Zeigler RG, Jones CJ, Brinton LA, Norman SA, Mallin K, Levine RS, Lehman HF, Hamman RF, Tremble AC, Rosenthal J, Hoover RN. "Diet and Risk of In Situ Cervical Cancer Among White Women in the United States." Cancer Causes and Control. 2:17-29. 1991.
11. Lasse DH, Savitz DA, Hamman RF, Baron AE, Brinton LA, Levine RS. "Invasive Cervical Cancer and Intrauterine Device Use." Int.J.Epidemiol. 20:865-70. 1991.
12. Levine RS and Doull J. "Global Estimates of Pesticide Mortality and Morbidity." Rev.Env.Contam.and Toxicol. 129:29-50. 1992.
13. Levine RS and Dolin P. "Pregnancy and Breast Cancer: A Possible Explanation for the Negative Association." J.Med.Hypoth. 38:278-283. 1992.
14. Levine, RS, Hennekens, CH, Jesse, MJ. Development of Blood Pressure in a Population-Based Cohort of Newborn Twins. BMJ. 1994; 308:298-302.
15. Levine, RS. "Practicing Without a Net." TIKKUN, Sep/Oct, 1995:65-73.
16. Levine, RS, Zhu, K, Braun, E, Baum, M, Gnepp, D. "Population-based Case Control Study of the Relationship Between Cigarette Smoking and Nasal Naso-pharyngeal Cancer." Cancer Causes & Control. In press.

## Abstracts and Presentations (\*Presented): 1990 to Present

- \*1. Fojas, A, Feldman, G, Hauben, M, Levine, R, Hodder, R, Marino, W. The Effect of Increased Attending supervision and Educational Intervention on the Practice of Influenza Vaccination by Medical Residents on Hospital Outpatients. Am. Rev.Resp. Dis. 141:A603. 1990.
2. Futterman, N, Zervis, G, Inba-Vazhau, G, Gupta, V, Levine RS, Hodder, RA, Ciaramida, SA. Near Misses in Thromboembolytic Therapy: The Need for Timely Delivery. Clin. Res. 38:703A. 1990.
- \*3. Levine, RS and Dolin, P. Halogenated Hydrocarbons and Human Cancer: A Reconsideration. International Society for Environmental Epidemiology. Buffalo, NY. June, 1991.
- \*4. Levine, RS, Kazi, I, Dolin, P, Futterman, N, Marino, W, Hodder, RA. Towards the Integration of Curative and Preventive Services for Internal Medicine Patients. American Public Health Association. Atlanta, GA. November, 1991. Abstracts:253.
- \*5. Levine, RS, Kazi, I, Dolin, P, Futterman, N, Marino, W, Hodder, RA. Integrating maternal preventive services at a well baby clinic. American Public Health Association. Abstracts:236.
- \*6. Levine, RS, Doull, J. Global Estimates of Pesticide Mortality and Morbidity. American Chemical Society. San Francisco, CA. 1992.
- \*7. Levine, RS. Medical effectiveness and quality assurance. Invited Lecture. Uniformed Services University of the Health Sciences. June 1993.
- \*8. Torres, T, Levine, RS, Carter, R. Intervention to increase the proportion of patients whose physicians advise regular physical activity. Prevention 94. Atlanta, GA. 1994.
9. Apollis, K, Nelson-Knuckles, B, Tate, H, Levine, RS. A family systems approach to the management of hypertension in African-Americans. Accepted for presentation. National Medical Association. August, 1994.
10. Turner, EA, Levine, RS, Federspiel, CF, Nelson-Knuckles, B, Wolff, S. Pharmacy payments for sickle cell diseases: Increases from 1980 to 1992. Submitted for presentation to APHA 123rd Annual Meeting, San Diego, CA. October, 1995.
- \*11. Levine, RS, Zhu, K, Braun, E, Baum, M, Gnepp, D. Population-based Case Control Study of the Relationship Between Cigarette Smoking and Nasal Naso-pharyngeal Cancer. Society of Epidemiological Research, Snowbird, UT. June, 1995.
12. Levine, RS, Zhu, K, Braun, E, Baum, M, Gnepp, D. Population-based Case Control Study of the Relationship Between Cigarette Smoking and Nasal Naso-pharyngeal Cancer. Am.J.of Epid. 131:S41, 1995.
- \*13. Zhu, K and Levine, RS. Population-based Case Control Study of the Relationship Between Cigarette Smoking and Liver Cancer, Society of Epidemiological Research, Snowbird, UT. June, 1995.
14. Levine, RS, Zhu, K, Braun, E, Baum, M, Gnepp, D. Population-based Case Control Study of the Relationship Between Cigarette Smoking and Primary Hepatic Cancer. Am.J.of Epid. 131:S61, 1995.

**BIOGRAPHICAL SKETCH**

Provide the following information for the key personnel in the order listed on Form Page 2.  
Photocopy this page or follow this format for each person.

NAME Vanessa C. Parker		POSITION TITLE Department of Preventive Medicine	
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)			
INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY
University of California - Sand Diego, San Diego, CA	B.S.	1982	Microbiology
California State University, Dominguez Hills, CA	M.A.	1989	Behavioral Sciences
University of Southern California	Ph.D.	1995	Preventive Medicine

RESEARCH AND PROFESSIONAL EXPERIENCE: Concluding with present position, list, in chronological order, previous employment, experience, and honors. Include present membership on any Federal Government public advisory committee. List, in chronological order, the titles, all authors, and complete references to all publications during the past three years and to representative earlier publications pertinent to this application. If the list of publications in the last three years exceeds two pages, select the most pertinent publications. DO NOT EXCEED TWO PAGES.

**PROFESSIONAL EXPERIENCE:**

11/93-Present Graduate Research Assistant, Drug Use and HIV-Risk Sexual Behaviors in Homeless Youth, Childrens Hospital Los Angeles, Division of Adolescent Medicine

07/93-Present Co-Principal Investigator, Adolescent Condom-Use Efficacy Among Urban Minorities, Charles R. Drew University of Medicine and Science

05/93-12/93 Project Manager, Gang Violence Prevention and Suppression Project, High-Risk Youth Project, Childrens Hospital-Division of Adolescent Medicine

06/92-12/93 Graduate Research Assistant, KCET/USC African American Smoking Prevention Project, University of Southern California

06/92-10/93 Sr. Research Associate, Women & HIV/AIDS Research Project, Charles R. Drew University of Medicine and Science

09/91-06/92 Graduate Research Assistant, Day One Community Partnership, University of Southern California

09/90-06/92 Program Manager, Tobacco Control Program, King-Drew Medical Center, Los Angeles, California

12/88-01/91 Staff Research Associate, California Heterosexual Partner Study, University of California, San Francisco

10/88-11/89 Program Manager, People Who Care Youth Center AIDS Education Project, Los Angeles, California

02/88-11/88 Medical Assistant Instructor, Watterson Career College, Los Angeles, California

05/88-09-88 Peer Ethnographic Interviewer, California State University, Long Beach, AIDS Education and Prevention Project, Long Beach, California

08/87-08/88 Minority Aids Educator, Long Beach Health Department, Aids Education and Prevention Project, Long Beach, California

06/86-09/87 Research Assistant, Cancer Research Consortium, Charles R. Drew University of Medicine and Science, Los Angeles, California

10/84-11/85 Medical Consultant, W.E. Thompson and Associates, Attorneys-at-Law, Washington, D.C.

## HONORS AND MEMBERSHIPS:

Distinguished Young Women of America, 1987

Certificate of Appreciation, County of Los Angeles, Department of Health Services, Sexually Transmitted Disease Program, November 1989

Certificate of Appreciation, Los Angeles Southwest College Women's Center, October 1989

Certificate of Appreciation, County of Los Angeles, Department of Health Services, Sexually Transmitted Disease Program

## SELECTED PUBLICATIONS:

1. Sussman, S., Parker, V., Crippens, D., Scholl, D., Elder P. "Empirical Development of Brief Smoking Prevention Videotapes Which Target African American Adolescents". International Journal of Addictions 1995;30(9):1141-1164.
2. Rohrbach, L., Fishkin, S., Mansergh, G., Parker, V., Johnson, C.A. "A Survey of Substance Use and Related Issues in Pasadena and Altadena, California". Technical Report, August 1994.
3. Parker, V., Montgomery, S., Kipe, MD, O'Guynn, S. "Tracking Homeless/Runaway Youth", Technical Report, March 1995.
4. Parker, V., Sussman, S., Herring, D., Crippens, D., et al. "Qualitative Development of Smoking Prevention Programming for Minority Youth" (Under Review)
5. Parker V., Sussman, S., "Cigarette Smoking Among Family and Friends of Urban African American Youth" (Under Review)
6. Parker, V., Sussman, S., Herring, D., Crippens, D., et al. "The relations of Ethnic Identification With Smoking Among Ethnic Minority Youth" (Under Review).
7. Parker, V., Montgomery, S., Kipke, M., O'Guynn, S., "Longitudinal Follow-up of Urban Homeless/Runaway Youth: Methodology" (In Preparation)
8. Parker, V., Ashley, M., Montgomery, S., "Sexual and Condom Use Behaviors Among African American Adolescents Living In An Inner-City Public Housing Development" (In Preparation)
9. Parker, V., Rabinovitz, S., Kipke, M., "The Practice of Violence Among Urban Homeless/Runaway Youth" (In Preparation)

**BIOGRAPHICAL SKETCH**

Provide the following information for the key personnel in the order listed on Form Page 2.

Photocopy this page or follow this format for each person.

NAME Linda Lue Pederson		POSITION TITLE Professor, Department of Epidemiology & Biostatistics	
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)</i>			
INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	YEAR(s)	FIELD OF STUDY
Brown University	B.A.	1964	Psychology
University of Iowa	M.A.	1966	Child Behavior
University Western Ontario	Ph.D.	1980	Epidemiology & Biostatistics

RESEARCH AND PROFESSIONAL EXPERIENCE: Concluding with present position, list, in chronological order, previous employment, experience, and honors. Include present membership on any Federal Government public advisory committee. List, in chronological order, the titles, all authors, and complete references to all publications during the past three years and to representative earlier publications pertinent to this application. If the list of publications in the last three years exceeds two pages, select the most pertinent publications. DO NOT EXCEED TWO PAGES.

**PROFESSIONAL EXPERIENCE:**

1994-Present Clinical Professor, Community Health & Preventive Medicine, Morehouse School of Medicine, Atlanta, GA

1994-1995 Professor, Epidemiology & Biostatistics, University of Western Ontario

1986-1991 Associate Director, Health Care Research Unit, University of Western Ontario

1984-1993 Associate Professor, Medicine, University of Western Ontario

1984-1994 Associate Professor, Epidemiology & Biostatistics, University of Western Ontario

1980-1984 Assistant Professor, Epidemiology & Biostatistics, University of Western Ontario

1980-1984 Assistant Professor, Medicine, University of Western Ontario

1979-1980 Research Associate, Medicine, Victoria Hospital/ University of Western Ontario

Winter 78 Teaching Assistant, Biostatistics II, Epidemiology & Preventive Medicine, University of Western Ontario

Fall 78 Teaching Assistant, Biostatistics I, Epidemiology & Preventive Medicine, University of Western Ontario

1973-1976 Research Assistant, Medicine, University of Western Ontario  
Programmer Coordinator, Smoking Withdrawal Program, Victoria Hospital  
Research Assistant, London Board of Education

1968-1975 Grader, Introductory Psychology Course, Psychology, Correspondence Division, University of Western Ontario

1968-1973 Consultant, Psychology, University of Western Ontario

1968-1973 Teaching Developmental Psychology, Extension & Summer School, University of Western Ontario

Oct. 1966- Research Associate, Psychology, London Psychiatric Hospital

May 1967

1964-1966 Research Assistant, Institute of Child Behavior & Development, University of Iowa

1963-1964 National Science Foundation Undergraduate Research Fellowship, Psychology, Brown University

**HONORS AND MEMBERSHIPS:**

Fellow, American College of Epidemiology, 1986

Member, Centre for Activity and Ageing, Lawson Research Institute of the St. Joseph's Health Centre and University of Western Ontario, 1993

Associate Member, Centre for Health Promotion, Banting Institute, University of Toronto, 1993-95



Steering Committee, "Working women's work-related health concerns survey", Industrial Disease Standards Panel, 1993

Board of Directors, Canadian Society for Epidemiology and Biostatistics, 1993

Reviewer, University of Toronto Press, 1992

Member, Advisory Board, Annals on Addiction; Journal published by the Publications Service of the University of Granada (Spain), 1992

Member, Editorial Board, Health Values, 1992

Advisory Board, Outcome Research for Independent Health Facilities, College of Physicians & Surgeons of Ontario, 1992

Advisory Board, Canadian Consensus on Physicians Intervention in Smoking Cessation, 1991

Member, Selection Committee for Chair, Department of Epidemiology & Biostatistics, University of Western Ontario, 1991

Member, Health Care Systems Review Committee, panel A., Ontario Ministry of Health, 1991-93

Coordinator, Department of Epidemiology & Biostatistics Seminar Services, 1990

Member-at-large, national Cancer Institute of Canada, 1990-98

Member, Ontario Health promotion Researchers and Practitioners Network Project Meeting, Ontario Prevention Clearinghouse Advisory Committee, June 4, 1990

Host, Ontario Health Promotion Researchers and Practitioners Workshop, Ontario prevention Clearinghouse, May 3, 1990

Member, Workshop on Health Promotion Research, Ontario Prevention Clearinghouse Advisory Committee, 1990

Member, Editorial Board, Women and health, 1989

Planning Committee, Adolescent Smoking Survey, Health and Welfare Canada, 1989-91

#### **SELECTED PUBLICATIONS:**

1. Ashley, M.J., Bull, S.B. and Pederson, L.L. Support among smokers and nonsmokers for restrictions on smoking. American Journal of Preventive Medicine, 1995 (in press).
2. Ostbye, T., Pomerleau, J., Speechley, M., Pederson, L.L. and Speechley, K. Correlates of body mass index in the 1990 Ontario Health Survey. Canadian Medical Association Journal, 1995, 152(11), 1811-1817.
3. Helmes, E., Hodsman, A., Lazowski, D., Bhardwaj, A., Crilly, R., Nichol, P., Drost, D., Vanderburgh, L. and Pederson, L. A questionnaire to evaluate disability in osteoporotic patients with vertebral compression fractures. Journal of Gerontology: Medical Sciences, 1995, 50A(2), M91-M98.
4. Bull, S.B., Pederson, L.L. and Ashley, M.J. Restrictions on smoking: Growth in population support between 1983 and 1991 in Ontario, Canada. Journal of Public Health Policy, 1994, 15(3), 310-328.
5. Bull, S.B., Pederson, L.L. and Ashley, M.J. Relationship of smoking status to changes in knowledge and attitudes concerning restrictions on smoking. Canadian Journal of Public Health, 1994, 85(2), 103-105.
6. Pederson, L.L., Bull, S.B., Ashley, M.J., Garcia, J.M. and Lefcoe, N.M. An evaluation of the work place smoking bylaw in the City of Toronto. American Journal of Public Health, 1993, 83(9), 1342-1345.
7. Turner, L.A., Pederson, L.L. and Ostbye, T. Health work force planning in the 90's, Part II: Enough in the right place at the right time? Healthcare Management Forum, 1993, 6(2), 23-30.
8. Turner, L., Ostbye, T. and Pederson, L.L. Work force planning in the 90's, Part I: Efficiency, economy and political will - the need for a new approach. Healthcare Management Forum, 1993, 6(1), 34-40.
9. Pederson, L.L., Bull, S.B., Ashley, M.J. and Kozma, D. Restrictions on smoking: Changes in knowledge, attitudes and predicted behavior in Metropolitan Toronto from 1983 to 1988. Canadian Journal of Public Health, 1992, 83(6), 408-412.
10. Pederson, L.L., Poulin, M., Lefcoe, N.M., Donald, A.W. and Hill, J.S. Does cigarette smoking affect the fitness of young adults?: Rationale and protocol for future research. The Journal of Sports Medicine and Physical Fitness, March 1992, 32(1), 96-105.

**BIOGRAPHICAL SKETCH**

Give the following information for the key personnel and consultants and collaborators. Begin with the principal investigator/program director. Photocopy this page for each person.

NAME <b>Kofi Alavi Semenya</b>	POSITION TITLE <b>ASSOCIATE DIRECTOR</b>
-----------------------------------	---

EDUCATION (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)

INSTITUTION AND LOCATION	DEGREE	YEAR CONFERRED	FIELD OF STUDY
University of Ghana, Legon, Ghana	B.S.	1971	Math & Physics
University of Ghana, Legon, Ghana	M.S.	1974	Statistics & Demographics
University of North Carolina	Ph.D	1980	Biostatistics

RESEARCH AND PROFESSIONAL EXPERIENCE: Concluding with present position, list, in chronological order, previous employment, experience, and honors. Key personnel include the principal investigator and any other individuals who participate in the scientific development or execution of the project. Key personnel typically will include all individuals with doctoral or other professional degrees, but in some projects will include individuals at the masters or baccalaureate level provided they contribute in a substantive way to the scientific development or execution of the project. Include present membership on any Federal Government public advisory committee. List, in chronological order, the titles, all authors, and complete references to all publications during the past three years and representative earlier publications pertinent to this application. DO NOT EXCEED TWO PAGES.

**EXPERIENCE**

1980 -1982      Assistant Professor of Biostatistics, Meharry Medical College, School of Medicine

1982 - 1986      Consultant in Biostatistics and Part-time Faculty Member, Meharry Medical College, SOM

1982 - 1986      Assistant Professor of Statistics, Department of Physics, Mathematics and Computer Science, Tennessee State University, Nashville, TN

1987 - Present      Associate Professor of Biostatistics, Cancer Control Research Unit and Department of Preventive and Community Dentistry, Meharry Medical College, Nashville, TN

**HONORS AND MEMBERSHIPS**

- Sigma Xi Scientific Society
- American Statistical Association
- Biometric Society
- Population Association of America

**PUBLICATIONS**

Koch, G.G., Grizzle, J.E., Semenya, K.A., and Sen, P.K. Statistical Methods for the Evaluation of Mastitis Treatment Data. Journal of Dairy Science, Vol. 61, No.6., 1987.

Semenya, K.A., Koch, G.G. Linear Models Analysis for Rank Functions of Ordinal Categorical Data. Proceedings of the Statistical Computing Section of the American Statistical Association, 1979.

Semenya, K.A., Koch, G.G. Compound Function and Linear Medal Methods for the Multivariate Analysis of Ordinal Categorical

Data. Institute of Statistics, Mimeo Series, No. 1323, UNC, Chapel Hill, NC., 1980.

Semenya, K.A., Koch, G.G. A Weighted Least Squares Strategy for Comparison of Populations Based on Grouped Survival Data. American Statistical Association - Proceedings of the Statistical Computing Section, 1981.

**BIOGRAPHICAL SKETCH**

Provide the following information for the key personnel in the order listed on Form Page 2.  
Photocopy this page or follow this format for each person.

NAME Samuel J. Shacks, Ph.D., M.D.	POSITION TITLE Associate Professor	May 20, 1939
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)		
INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)
Arkansas State AM&N College, Pine Bluff, Ark.	B.S.	1960
University of California, Irvine, CA	Ph.D.	1972
University of California, Irvine, CA	M.D.	1977
Harbor/UCLA Medical Center, Torrance, CA	Fellowship	1981-83
		FIELD OF STUDY
		Biology Chemistry
		Biology
		Medicine
		Immuno/Allergy

RESEARCH AND PROFESSIONAL EXPERIENCE: Concluding with present position, list, in chronological order, previous employment, experience, and honors. Include present membership on any Federal Government public advisory committee. List, in chronological order, the titles, all authors, and complete references to all publications during the past three years and to representative earlier publications pertinent to this application. If the list of publications in the last three years exceeds two pages, select the most pertinent publications. **DO NOT EXCEED TWO PAGES.**

**Appointments/Positions:**

1972-73 Research Fellow, Medicine, Robert B. Brigham Hospital, Harvard Medical School, Boston, Massachusetts.

1973-74 Research Fellow in Immunology, Department of Microbiology and Immunology, University of California, Los Angeles, School of Medicine.

1977-80 Pediatrics Residency, Martin Luther King, Jr. General Hospital, Los Angeles, California.

1980-1992 Assistant Professor, Charles R. Drew University of Medicine and Science, Martin Luther King, Jr., General Hospital, Department of Pediatrics, Los Angeles, California.

1981-83 MARC Faculty Fellowship in Pediatric Immunology, Division of Immunology and Allergy, Harbor-UCLA Medical Center, Torrance, California.

1991-Present Chief, Pediatric Immunology/Rheumatology, Department of Pediatrics, King/Drew Medical Center, Los Angeles, California.

1992-95 Associate Professor I, Charles R. Drew University of Medicine and Science, Martin Luther King, Jr., General Hospital, Department of Pediatrics, Los Angeles, California.

1995-Present Associate Professor II, Charles R. Drew University of Medicine and Science, Martin Luther King, Jr., General Hospital, Department of Pediatrics, Los Angeles, California.

**Experiences:**

1983-87 MARC Review Committee, NIH/NIGMS, Bethesda, Maryland.

1984-Present Director, MARC and MBRS Programs, Charles R. Drew University of Medicine & Science, Los Angeles, California.

1986-Present Comprehensive Sickle Cell Centers Parent Review Committee, NIH/NHLB, Bethesda, Maryland.

1987-1992 Associate Dean for Research, Charles R. Drew University of Medicine and Science, Los Angeles, California.

1987-Present Association of Minority Health Professions Schools (AMHPS), Washington, D.C.

1987-92 Liaison/Coordinator for AMHPS/NIH Initiatives, National Cancer Institute, National Institutes of Health, Bethesda, Maryland.

1987-Present Liaison Officer, Department of Defense, National Association for Equal Opportunity in Higher Education, Washington, D.C.

1989 Their Committee: State of the Nation's Health Research Facilities Infrastructure, National Academy of Science, Washington, D.C.

1990-Present Consumer Representative, Immunology Devices Panel Food & Drug Administration, Rockville, Maryland.

- 1990-1991 Member, Sickle Cell Disease Task Force for the National Health, Lung, and Blood Institute (NHLBI) National Institutes of Health, Bethesda, Maryland.
- 1990-Present Member, Executive Board of Directors, National Cancer Control Research Network, Inc., National Cancer Institute, NIH, Bethesda, Maryland.
- 1990-91 Partnership Member, NSF-Alliances for Minority Participation Program, California State University Dominguez Hills, Los Angeles, California (Planning Grant).
- 1990-91 Member, Health Technology Study Section, Agency for Health Care Policy and Research/DHHS/PHS, Rockville, Maryland.

## HONORS:

- 1972 Ph.D. Valedictory Speaker and Outstanding Graduate Student, University of California, Irvine, California.
- 1978-79 Outstanding Achievement, Department of Pediatrics, Martin Luther King, Jr., Hospital, Los Angeles, California.
- 1981 Travel Grant Award Recipient, American Academy of Pediatrics, Section on Allergy and Immunology.
- 1987 Distinguished Alumni Citation of the Year Award, National Association for Equal Opportunity In Higher Education, Washington, D.C.
- 1987 Outstanding Performance/Service in Medicine, University of Arkansas at Pine Bluff, Arkansas.
- 1988 Alumni of the Year Award, University of California, Irvine, Irvine, California.
- 1989 Chair, Research Group, Association of Minority Health Professions Schools, Washington, D.C.

## Publications:

1. Granger, G.A., Shacks, S.J., Williams, T.W. and Kolb, W.P.: Lymphocyte in vitro cytotoxicity; specific release of lymphotoxin like materials from tuberculin sensitive lymphoid cells. *Nature* 211:115-7, 1969.
2. Shacks, S.J. and Granger, G.A.: Studies on in vitro models of cellular immunity. *J. Reticulohistocytol.* 10:28-49, 1971.
3. Shacks, S.J., Chiller, J. and Granger, G.A.: The in vitro role of thymus dependent cells in DNA synthesis and LT secretion by PHA-stimulated mouse lymphoid cells. *Transpl. Proceed* 4:303-7, 1972.
4. Shacks, S.J., Chiller, J. and Granger, G.A.: Studies on in vitro models of cellular immunity: The role of T and B cells in the secretion of lymphotoxin. *Cellular Immunol.* 7:313-21, 1973.
5. Brosman, S., Hausman, M. and Shacks, S.J.: Studies on the immune status of patients with renal adenocarcinoma. *Jour. Urol.* 114:373-80, 1975.
6. Brosman, S., Hausman, M. and Shacks, S.J.: Immunologic alterations in patients with prostatic carcinoma. *Jour. Urol.* 113:841-45, 1975.
7. Shacks, S.J. and Heiner, D.C.: Allergy to Breast Milk. *Clinics in Immunol. and Allergy.* 2(1):121, 1982.
8. Alfred, L.J., Ghoneum, M., Wojdani, A. and Shacks, S.J.: Alterations in NK activity and T-cell subsets during the development of chemically induced tumors: Role of biological response modifiers (BRMS). *Immunobiol.* 167, 1984.
9. Shacks, S.J., Heiner, D.C., Bahna, S.L. and Horwitz, C.A.: Increased Serum IgG4 Levels in Acute Epstein-Barr Viral Mononucleosis. *Annals of Allergy*, Vol. 54, Number 4, 1985.
10. Shacks, S.J. and Johnson, C.S.: Serum Concentration of Total IgG and IgG4 in Sickle Cell Anemia. *American Society of Hematology Blood*, 66, Suppl. 1, 1986.
11. Shacks, S.J.: Reaching Hard-to-Reach Populations. *Proceedings of the 4th National Environmental Health Conference* (pages 265-69), U.S. Dept. of Health and Human Services, PHS, San Antonio, Texas June 20-23, 1989.
12. Taylor, S.C. and Shacks, S.J.: Lymphokine and NK Cell Activity in Sickle Cell Disease: Pediatric Asthma Allergy and Immunology. Vol. 3 #4, 1989.
13. Taylor, S.C., Shacks, S.J., Villicana, S.M., Olivares, J. and Dinkins, A.: Interferon Production In Sickle Cell Disease: Lymphokine Research, Vol. 9, No. 3: 415-423, July 1990.
14. Taylor, S.C., Shacks, S.J., Villicana, S.M., Olivares, J. and Dinkins, A.: Lymphocyte Blastogenic Responses in Sickle Cell Disease: Immunological Investigations, Vol. 20, Iss. 5: 645-655, 1991.
15. Taylor, S.C., Shacks, S.J., Mitchell, R.A.: Mononuclear Cell Profiles in Sickle Cell Disease: Regional Meetings-American Federation for Clinical Research, Carmel, CA, February 8-11, 1995.
16. Taylor, S.C., Shacks, S.J., Mitchell, R.A., and Banks, Aaron: Serum Interleukin-6 Levels in the Steady State of Sickle Cell Disease, *Journal of Interferon and Cytokine Research*, Vol. 15, Issue 12: 1061-1064, 1995.
17. Taylor, S.C., Shacks, S.J., Mitchell, R.A.: In vitro lymphocyte blastogenic responses and cytokine production in sickle cell disease patients with acute pneumonia, *Pediatric Infectious Disease Journal*, Vol. 15, Issue 4: 340-344, 1996.

CONTINUATION PAGE: STAY WITHIN MARGINS INDICATED

**BIOGRAPHICAL SKETCH**

Provide the following information for the key personnel in the order listed on Form Page 2.  
Photocopy this page or follow this format for each person.

NAME Beverly D. Taylor, MD		POSITION TITLE Associate Professor & Residency Director	
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)			
INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY
Fisk University, Nashville, TN	B.A.	1972	Biology
Meharry Medical College, Nashville, TN	M.D.	1976	Medicine
Meharry Medical College, Nashville, TN	Post Grad. Training	1976-80	Family Med. & Preventive Med.

RESEARCH AND PROFESSIONAL EXPERIENCE: Concluding with present position, list, in chronological order, previous employment, experience, and honors. Include present membership on any Federal Government public advisory committee. List, in chronological order, the titles, all authors, and complete references to all publications during the past three years and to representative earlier publications pertinent to this application. If the list of publications in the last three years exceeds two pages, select the most pertinent publications. DO NOT EXCEED TWO PAGES.

**PROFESSIONAL EXPERIENCE:**

- 1986 Associate Professor, Clinical Community Health/Preventive Medicine, Department of Community Health/Preventive Medicine, Morehouse School of Medicine, Atlanta, GA.
- 1986 Director, Public Health/Preventive Medicine Residency Program, Department of CH/PM, Morehouse School of Medicine, Atlanta, GA
- 1985 Director Undergraduate Medical Education, Family Medicine Clerkship, Department of CH/FP, Morehouse School of Medicine, Atlanta, GA.
- 1984-85 Assistant Professor, Department of CH/FP, Morehouse School of Medicine, Atlanta, GA
- 1983-84 Part-time association with Med First Centers, Atlanta, GA
- 1983-84 Part-time association with Med First Centers, Atlanta, GA
- 1981-82 Private Practice, Birmingham, Alabama
- 1981 Assistant Professor - Department of Family Medicine and Community Medicine, Meharry Medical College, Nashville, TN
- 1980 Instructor - Joint appointments in Department of Family Medicine and Community Medicine, Meharry Medical College and Tennessee Department of Public Health, Mid-Cumberland Region.
- 1979-80 Chief Resident, Family Medicine Residency Program, Meharry Medical College
- 1976-80 Resident-Family Medicine & Preventive Medicine Residency Program, George Hubbard Hospital, Nashville, TN
- 1972-74 Counselor/Teacher - Biology - Upward Bound Program, Fisk University, Nashville, TN

**SELECTED PUBLICATIONS:**

- Taylor, BD, Glazner, HK; Young, "Primary prevention of Hypertension: New Directions for the Nation". Presented at the American Occupational Health Conference, April 25-30, 1993.
- Sung, JFC; Taylor B, et al. Maternal Marital Status and Racial Differences in Infant Mortality: A Georgia population based study (Abstract accepted for Prevention '92. Baltimore, MD Poster Presentation).
- Fain M, Taylor BD, Johnson JC, Williams MP, Moss SE, Cultural and Linguistic Diversity in African American Alzheimer's Patients. Presented at American Speech-Language Hearing Association Annual Meeting, Marriott Marquis Hotel, Atlanta, GA, November 23 1991.

4. Taylor, BD, Improving Your Risks - A look at lifestyle interventions for the working woman. Presented at the Georgia Northwest Council of Girl Scouts. Unity Presbyterian Church, Decatur, GA, September 1991.
5. Blumenthal, DS and Taylor, BD. The Need for Black Specialists in Preventive Medicine. American Journal of Preventive Medicine, 1990; 6(6), 330-332.
6. Taylor, BD. "Utilization of Preventive Medicine Residents in the Teen Clinical Preventive Medicine Service at the Fulton County Health Department." Presented in the Maternal and Child Health/Teenage Pregnancy Section of the National AHEC Conference, Louisville, Kentucky, June 11-14, 1989.
7. Taylor B, Griffith P, Sung JFC and Densler M. "Characteristics of Alzheimer's Disease in Blacks". Presented to the Georgia Regional Conference on Aging. September 28, 1989.
8. Taylor B, Griffith P, Sung JFC, and Densler M. "Alzheimer's Disease Investigation at a Community Hospital", Atlanta, Georgia. Presented at Georgia Rural Health Conference. Helen, Georgia, 1988.
9. Blumenthal DS, and Taylor BD. "If I Ran the Zoo", an example of required ambulatory clerkships in the senior year. Presented at the Society of Teachers in Family Medicine, Spring Conference, April 1, 1985, Atlanta, Georgia.
10. Mims A, Sung JFC, Taylor BD, et al. The Effectiveness of personal Letters to improve the influenza Immunization Rate in Geriatric Patients.

**BIOGRAPHICAL SKETCH**

Provide the following information for the key personnel in the order listed on Form Page 2.  
Photocopy this page or follow this format for each person.

NAME <b>Ling Y Wu, M.D., Ph.D.</b>		POSITION TITLE <b>Faculty Researcher</b>	
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)			
INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY
Shanghai Medical Uni., Shanghai, China	M.D.	1982	Medicine
University of Berkeley, Berkeley, CA	MPH	1992	Maternal and Child Health
Johns Hopkins University, Baltimore, MD	Ph.D.	1996	Reproductive Health

RESEARCH AND PROFESSIONAL EXPERIENCE: Concluding with present position, list, in chronological order, previous employment, experience, and honors. Include present membership on any Federal Government public advisory committee. List, in chronological order, the titles, all authors, and complete references to all publications during the past three years and to representative earlier publications pertinent to this application. If the list of publications in the last three years exceeds two pages, select the most pertinent publications. **DO NOT EXCEED TWO PAGES.**

**EXPERIENCE**

1995 Intern, Family Health International, Division of Contraceptive Use and Epidemiology.  
1992-1995 Johns Hopkins University, Department of Population Dynamics. Baltimore, MD.  
1992 Visiting Physician, Grady hospital, Department of Family Planning Clinic. Atlanta, GA.  
1982-1991 Physician, Shanghai Public Health Center. Shanghai, China.

**HONORS**

Fellowship, Hewlett Foundation, 1992-1996  
Scholarship, Starr Foundation, 1991-1992  
Honored thesis, "Family Planning Programs and their Future at University of Berkeley", 1992  
Outstanding Physician, Shanghai Public Health Center, 1986  
Honored thesis, "Risk Factors of Breast Cancer", Shanghai Medical University, 1982



**BIOGRAPHICAL SKETCH**

Provide the following information for the key personnel in the order listed on Form Page 2.  
Photocopy this page or follow this format for each person.

NAME	POSITION TITLE
Kangmin Zhu	Research Assistant

EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)

INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY
Tongji Medical University, Wuhan, PRC	M.D.	1982	
Tongji Medical University, Wuhan, PRC	M.P.H.	1985	Epidemiology
University of Washington, Seattle, WA	Ph.D.	Present	Epidemiology

RESEARCH AND PROFESSIONAL EXPERIENCE: Concluding with present position, list, in chronological order, previous employment, experience, and honors. Include present membership on any Federal Government public advisory committee. List, in chronological order, the titles, all authors, and complete references to all publications during the past three years and to representative earlier publications pertinent to this application. If the list of publications in the last three years exceeds two pages, select the most pertinent publications. DO NOT EXCEED TWO PAGES.

**PROFESSIONAL EXPERIENCE:**

1992 - Present	Research Assistant, Social Development Research Group, University of Washington, Seattle, WA
1990 - 1991	Research Assistant, Children's Hospital and Medical Center, Seattle, WA
1989 - 1990	Research Assistant, Department of Epidemiology, University of Washington, Seattle, WA
1987 - 1988	Assistant Professor, Tongji Medical University, Wuhan, PRC
1985 - 1987	Teaching Assistant, Tongji Medical University, Wuhan, PRC

**HONORS AND MEMBERSHIPS:**

The third-class award for the studies on hypertension granted by Hubei province Government, PRC, 1988

Chinese Medical Association, PRC, 1986 - 88

Hubei Epidemiologic Association, Hubei, PRC, 1986-1988

Society for Epidemiologic Research, USA, 1993 - present

Outstanding Student, Tongji Medical University, PRC, 1981

Outstanding Student, Tongji Medical University, PRC, 1980

Outstanding Student, Tongji Medical University, PRC, 1979

Outstanding Student, Tongji Medical University, PRC, 1978

**SELECTED PUBLICATION:**

1. Zhu K. A discussion of logical methods in research on causality between smoking and lung cancer. *Medicine and Philosophy* 1986;7:10-2.
2. Zhu K., He S., Pan X., Zheng X., Gu Y. The relation of urinary cations to blood pressure in boys aged seven to eight years. *Am J Epidemiol* 1987;126:658-63.
3. Zhu K., He S., Pan X., Zheng X., Gu Y. The relationship between blood pressure and sodium, potassium, calcium and magnesium in the urine. *Chinese J Epidemiol* 1987;8:9-13.
4. Zhu K., He S. The estimation of population attributable risk fraction in case-control studies. *Guowai Yixue* 1987;4:198-204.
5. Zhu K., He S., Pan X. The logistic regression analysis of urinary cations in relation to blood pressure in children. *J Clin Cardiol* 1987;3:223-5.
6. Zhu K., He S., Pan X., Zheng X., Gu Y., Zhang Y., Shi L., Huang R. A study of variables in relation to blood pressure among boys by factor analysis. *Chinese J Prev Med* 1988;3:169.
7. Zhu K., He S. The intrapopulation studies on the relationship between sodium and hypertension. *Prog in Epidemiol* 1988;5:295-307.
8. Zhu K., He S. The estimation of relative risk in case-control studies. *Chinese Hlth Stat* 1989;6:25-8.
9. Zhu K., Shi L., Huang M., Li G., Zhan Z. A study of the relationship between urinary cations and blood pressure among old people in Wuhan. *Acta Tongji University* 1989;3:207-8.
10. Zhu K., Daling J., Mueller B., Sherman K. The association of HIV infection and lymphoma occurrence: an analysis using SEER data (abstract). *Am J Epidemiol* 1991;134:780.
11. Zhu, K., Psaty, B. Sodium and blood pressure: The puzzling results of intrapopulation epidemiologic studies. *Med Hypotheses* 1992;38:120-4.
12. Zhu, K. "Sick building syndrome": an inappropriate term. *J Occup Med* 1993;35:752.
13. Zhu K., Weiss, NS., Schwartz, SM., Daling JR. Assessing the relationship between marital status and cancer incidence: methodological considerations. *Cancer Causes and Control* 1994;5:83-7.

**APPENDIX B1**

Sherry Crump, MD, MPH

~~CONFIDENTIAL~~

Protocol  
Barriers to Screening Mammography Utilization  
Among Black Women at Grady Memorial Hospital

I. ABSTRACT

Breast cancer is the second leading cause of cancer deaths among women in the United States today. Mortality from this cancer is disproportionately higher among Black women as compared to White women. This difference is partly related to the late stage of the disease at diagnosis. For this reason, encouraging Black women to receive early screening and treatment is essential. Despite the fact that the survival rate for localized breast cancer is relatively high, and that mammography has been shown to be effective in the early detection of the cancer, screening rates among women remain low. At Grady Memorial Hospital, a major urban hospital providing services to disadvantaged and minority populations in Atlanta Georgia, an estimated 33% of the women patients fail to follow-through with their screening mammogram appointments. No study has been performed to delineate the factors that are associated with noncompliance with screening mammogram recommendations among these women. The purpose of this study is to specifically identify the psychological, social, and systemic factors that are associated with noncompliance with screening mammogram appointments among Black women at Grady Memorial Hospital. A case-control study will be used to differentiate these factors in women who do not comply with their mammogram appointments (cases) from those who do (controls). A total of 640 Black women 35 years of age and older who have appointments for screening mammography with the Grady Memorial Radiology Department between January 2, 1996 and March 29, 1996 will be selected to participate in the study (320 cases, 320 controls). Data will then be collected by telephone interview using a pre-tested questionnaire and will be analyzed using bi-variate analysis and logistic regression. The outcome variable to be measured is the receipt of a screening mammogram by the patient. The predictor variables to be measured will include: socio-demographics; past and current medical history; knowledge, attitudes, beliefs, and practices surrounding breast cancer prevention and control; reasons for not keeping the current mammogram appointment; interactions with family, friends and primary care provider; delayed time interval between the ordering date and appointment date for the mammogram; the breast health information communicated to the woman by the provider; and receipt of a telephone call reminder. By identifying potential barriers to screening mammogram utilization among inner city Black women, effective interventions can be developed to promote compliance with screening mammogram recommendations and to ultimately improve the survival rate of women with breast cancer in this population.

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## II. PROBLEM IDENTIFICATION AND DEFINITION

Breast cancer is the second leading cause of cancer deaths among women in the United States today. In 1995, an estimated 182,000 women will be diagnosed with invasive breast cancer.<sup>1</sup> In this same year, an estimated 46,000 breast cancer-related deaths will occur. Black women die from breast cancer at a disproportionately high rate as compared to White American women. Although the incidence of breast cancer is higher among White women than Black women (109.1/100,000 vs. 87.8/100,000), the mortality is actually higher for Black women (30.4/100,000 vs. 27.5/100,000).<sup>2</sup>

Survival from breast cancer is closely linked to the stage of the disease at diagnosis. The overall 5-year survival rate is 94% for localized breast cancer, but only 18% if distant metastasis has occurred.<sup>1</sup> The 5-year survival rate for all stages of breast cancer is higher for White women than for Black women - 82% vs. 66% in 1983-1990.<sup>1</sup> Studies have shown that Black women have later stages of breast cancer at diagnosis as compared to White women, which partially accounts for the higher mortality rate in this group of women.<sup>3,4,5</sup> For this reason, encouraging Black women to receive early screening and treatment is imperative.

Mammography is effective in the early detection of breast cancer, reducing mortality by 30% to 40% among women 50 years old and above when combined with clinical examination.<sup>6,7</sup> Most major authorities recommend mammography screening once a year for women 50 and older.<sup>8</sup> Some authorities recommend that women 40 to 49 years old receive a screening mammogram every 1 to 2 years, but there is still disagreement about the role of screening mammography in this age group.<sup>8</sup> Despite these recommendations, breast cancer screening rates still remain low. Results from the 1987 Behavioral Risk Factor Surveillance System (data from 33 states) showed that only 29% of U.S. women 50 years old and above had received a mammogram in the previous year.<sup>9</sup> The annual National Health Interview Survey revealed that in 1990, only 33% of women 40 and older had received a screening mammogram in the previous year.<sup>10</sup>

Many studies have been performed to determine the reasons that breast cancer screening rates are suboptimal, or specifically, to address the barriers to complying with breast cancer screening recommendations. Factors associated with noncompliance to screening recommendations have included fear,<sup>11,12,13</sup> embarrassment,<sup>13,14</sup> lack of knowledge of screening recommendations,<sup>11,13,14</sup> lack of a recommendation by a physician,<sup>3,5,6</sup> lack of a regular physician,<sup>14,15</sup> cost of the mammogram,<sup>4,5,6</sup> lack of insurance,<sup>6</sup> time constraints,<sup>13,16</sup> and transportation problems.<sup>13</sup>

Grady Memorial Hospital is a primary, secondary, and tertiary health care center which provides services to disadvantaged and minority populations in Atlanta, Georgia. An estimated 13,000 women 35 years of age and older have mammogram scheduled at this institute each year (unpublished source). Of these women, 3000 fail to follow-through with the appointment. No study has been done to evaluate the factors associated with noncompliance for screening mammogram recommendations among these women.

### III. GOALS AND OBJECTIVES

The goal of this study is to determine the barriers to complying with screening mammography recommendations among Black women 35 years of age and older. By identifying these barriers, effective interventions can be developed to promote early mammography screening and to ultimately improve the survival rate of Black women diagnosed with breast cancer.

The specific objectives of the study are to:

1. identify and characterize women 35 years of age and older at Grady Memorial Hospital who do not keep their screening mammogram appointments.
2. identify the psychological, social, and systemic factors that are associated with noncompliance with screening mammogram appointments among these women.

### IV. RESEARCH HYPOTHESES

1. At Grady Memorial Hospital, the psychological and social characteristics of women who do not keep their mammogram appointments are different from those of women who do.
2. At Grady Memorial Hospital, women who do not keep their appointments experience different systemic issues than women who do keep their appointments.

### V. METHODS

#### 1. Study design - case-control

#### 2. Study Population

##### a. Inclusion criteria

- Black women 35 years of age and older
- Women who have an appointment for screening mammography with the Grady Memorial Radiology Department between January 3, 1996 and March 29, 1996.

##### b. Exclusion criteria

Patients:

- with no known telephone number or contact telephone number(s)
- who do not speak English
- who have a history of breast cancer
- who were referred for mammography because of breast signs or symptoms

### 3. Sampling

#### a. method - simple random sample

A case-control study design will be used to focus on Black women 35 years of age and older who have screening mammogram appointments at Grady Memorial Hospital between January 3, 1996 and March 29, 1996. Mammogram requisitions from the radiology department will be reviewed to select women who qualify for the study. Information on the requisitions includes the clinic from which the requisition originated, the name and age of the patient, breast problems of the patient, the date of the mammogram appointment, and the date of the mammogram requisition. Patients will not be considered for the study if they have a history of breast cancer, or if they were referred for mammography secondary to breast signs or symptoms.

Cases will include women who have screening mammogram appointments scheduled between January 3, 1996 and March 29, 1996 at Grady, but who fail to keep their appointment. Controls will include women who have screening mammogram appointments also scheduled between January 3, 1996 and March 29, 1996 at Grady, but who do keep their appointments. Women who do not keep their mammogram appointments with Grady but indicate that they have received the mammogram at another institute will still be classified as cases. During analysis, receiving a mammogram appointment at an institute outside of Grady will be used as a predictor of not complying with Grady screening mammogram appointments. Cases and controls will be matched by day of appointment.

During the interview with selected study participants, true cases and controls will be verified by obtaining information on the age, race, and employment location of the patient. History of breast cancer or breast signs or symptoms will be ascertained at this time as well. After the initial interview, individuals who do not meet the inclusion criteria or who meet any of the exclusion criteria will be dropped from the study.

Each week of the study period, the names, addresses, and telephone numbers of women who have mammogram appointments in the upcoming week will be listed. Women who clearly meet the exclusion criteria (V.2.b.) will not be included on the list. Addresses and telephone numbers will be obtained through the Grady billing and appointment system (MediPack). For each week, women who qualify as either cases or controls will be identified. After enumerating each individual on both the case and control lists, a subset of individuals for the study will be selected by simple random

sampling using a table of random numbers. A total of 24 women (12 cases and 12 controls) will be selected each week during the study period. Women who have been selected for the study will be interviewed by telephone using a pre-tested questionnaire. Women who can not be reached by telephone after 5 attempts will be dropped from the subject pool. Prior to the telephone interview, letters will be sent to the cases and controls describing the purpose of the study.

Immediately following the telephone interview, women in the case group will be encouraged to reschedule their screening mammogram appointments. During the dialogue between the interviewer and the study participant, information on the importance of mammography screening will be emphasized. The participant will then be offered assistance in re-scheduling the appointment. Written information on breast cancer screening will be offered to all study participants and sent to those women who request it.

At the conclusion of the study, information will be obtained to determine if the phone call reminder prompted women in the case group to reschedule and receive their mammogram. The rate of screening mammography utilization of a subset of the cases will be compared to the rate of a subset of women who (in the prior 3 month period) did not keep their appointment and who were not selected for the study. Lists of both actual and potential study participants (generated over the course of the study) will be used to enumerate the women. Simple random sampling using a table of random numbers will be used to select new cases (women who did not keep their appointments and who participated in the study) and new controls (women who did not keep their appointments and who did not participate in the study). By reviewing information in the Grady computer system, the receipt of screening mammogram by women in the new case and control groups will be determined.

#### b. Sample size

##### Part 1:

calculation:

- null hypothesis #1 - There is no difference between psychological and social characteristics in women who do not keep their screening mammogram appointments and those who do.
- null hypothesis #2 - There is no difference between systemic issues experienced by women who do not keep their screening mammogram appointments and those who do.
- statistical test - z statistic
- alpha (two-tailed) - 0.05
- beta - 0.20
- power - 0.80

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- odds ratio - 2.65
- control:case - 1:1
- target sample size - 146 cases, 146 controls
- estimated phone contact rate - 70%
- estimated response rate - 65%
- minimal sample size - 320 cases, 320 controls

#### Part 2:

##### calculation:

- (null hypothesis #3) - A telephone call reminder will not prompt women who do not keep their screening mammogram appointments to subsequently reschedule and receive their mammogram within a 6 month period.
- statistical test - z statistic
- alpha (one-tailed) - 0.025
- beta - 0.20
- power - 0.80
- risk ratio - 1.5
- control:case - 1:1
- target sample size - 140 cases, 140 controls
- minimal sample size - 140 cases, 140 controls

#### 4. Measurements

##### a. Data collection method and instrument -

The Grady computer system will first be used to determine if women received the screening mammogram. Data will then be collected by telephone interview using a pre-tested questionnaire. Prior to the interview, letters at the 4th-5th grade level will be sent to the selected study participants in order to inform them of the nature of the study and of the forthcoming telephone call. For the portion of the study which determines the impact of the telephone call reminder, demographics of the women who did not keep their appointments and who did not participate in the study will be obtained from the Grady computer system.

A log will be kept of all the women selected for the study. This log will include: the name, address, and phone number of each woman; the date of the mammogram requisition; the name of the ordering clinic; date of the mammogram appointment; the number of telephone contacts with each woman and the outcome of the contacts; whether or not the participant has rescheduled the appointment; and the name of the interviewer.

##### b. Method of consent and confidentiality -

Verbal consent will be obtained from the potential participants on the telephone after 1) describing the purpose, procedures, and benefits of the study and 2) after assuring them that participation in the study is completely voluntary and that confidentiality will be maintained. The confidentiality of the participants will be protected by excluding their names, addresses, and phone numbers from the questionnaire. No participant will be able to be identified during analysis of the data. When questioning the participant on systemic concerns, names of health care providers or other staff members will not be solicited.

c. Variables -

Outcome variable - The outcome variable to be measured is the receipt of a screening mammogram by the patient.

Predictor variables - The psychological and social predictor variables to be measured will include: socio-demographics, insurance status, type of transportation, past and current medical history, knowledge of breast cancer risk factors and screening recommendations, attitudes and beliefs surrounding breast cancer and screening recommendations, prior breast cancer screening practices, reasons for not obtaining a mammogram in the past (if applicable), reasons for not keeping the current mammogram appointment (for cases only), interactions with family and friends, interactions with primary care provider, satisfaction with Grady Memorial Hospital services, and receipt of a screening mammogram at an institute other than Grady. The systemic predictor variables to be measured include: the Grady clinic from which the screening mammogram was ordered, the time interval between the date the screening mammogram was ordered and the date of the appointment, and the information that the woman received at the time the mammogram was ordered on the purpose of the screening mammogram. The interventional predictor variable to be measured is the receipt of a telephone call reminder.

Potential confounding variables - One potential confounding variable is the occurrence of any breast cancer prevention and control media campaigns or projects at the time of the study. In addition, during the measurement of the impact of the telephone call reminder, the influence of the Grady staff on the study participants can be a potential confounder.

d. Methods of data quality control -

The questionnaire will be pretested and adjusted twice prior to implementation of the study. Six weeks prior to the study and on two separate occasions, 20 women with screening mammogram will be selected for the pretest (10 women who did not keep their appointments and 10 women who did). Pretesting will include data collection, data entry, and limited analysis.

Interviewers and the data entry person will be appropriately trained for data collection and data entry, respectively. A breast health education script will be developed for use by the interviewers during the study interview.

## VI. STATISTICAL ISSUES

### 1. Analysis -

The frequency distribution of the predictor and outcome variables will be measured in proportions. Bi-variate analysis will be first performed to measure the magnitude of the associations between these variables using the odds ratio and the chi square test of association and confidence intervals will be used to measure statistical significance. Logistic regression will be used to control for confounding variables. EPI INFO and SAS analytical software packages will be used for data analysis.

### 2. Interpretation -

The results obtained in this study will only be generalizable to Black inner city women who already have screening mammogram appointments scheduled. Selection bias may occur in that only women who are able to be contacted by telephone will be able to participate in the survey.

## VII. LOGISTICS

### 1. Already available (in-kind) resources, personnel, facilities

- a. Grady Memorial Hospital
- b. Computer and printer
- c. EPI INFO and SAS analytical software packages
- d. Office space

### 2. Required (needed) resources, personnel, facilities

- a. Data entry person (1)
- b. Interviewers (2)
- c. Standard office supplies
- d. Printing expenses
- e. Postage

### 3. Budget (see attached worksheet)

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## APPENDIX B2

## PRESENTATIONS

- October 1995      Barriers to Screening Mammography Utilization  
Among Black Women at Grady Memorial Hospital -  
A Study Design. Morehouse Medical Treatment  
Effectiveness Center Advisory Group Meeting,  
Atlanta, Georgia.
- March 1996        Barriers to Screening Mammography Utilization  
Among Inner-City Black Women - A Study Design.  
Seventh Annual Symposium of the  
Drew/Meharry/Morehouse Consortium Cancer Center,  
Atlanta, Georgia.
- June 1996         Barriers to Screening Mammography Utilization  
Among Inner-City Black Women - A Study Design.  
Georgia State Medical Association Annual Meeting,  
Hilton Head, South Carolina.
- September  
1996                Barriers to Screening Mammography Use Among Urban  
African-American Women. American Psychological  
Association Women's Health Conference, Washington,  
D.C.
- November  
1996  
(Pending)          Barriers to Screening Mammography Utilization  
Among Inner-City Black Women. American Public  
Health Association Annual Meeting, New York, New  
York.

## APPENDIX B3



## VIII. WORK SCHEDULE

<u>Deadline</u>	<u>Activity</u>
June 1, 1995	1) Begin development of questionnaire 2) Begin search for data entry person and interviewers
July 31	1) Complete development of questionnaire 2) Write computer program for data entry 3) Hire data entry person and interviewers
August 31	1) Train interviewers 2) Pretest questionnaire 3) Revise questionnaire as needed
November 1	1) Begin recruiting and interviewing subjects
October 1	1) Begin data entry
April 30, 1996	1) Complete recruiting and interviewing subjects 2) Complete data entry 3) Begin to analyze data
June 30	1) Complete data analysis 2) Begin writing report
August 31	1) Complete writing report 2) Submit paper for publication

## APPENDIX C


# **ELECTROMAGNETIC FIELD EXPOSURE AND THE OCCURRENCE OF BREAST CANCER IN WOMEN.**

## **INTRODUCTION**

Over the past decades there has been numerous reports of modest to acute associated risk for the occurrence of different kinds of cancer due to exposure to EMF (Anthony and Thomas, 1970; Menck and Henderson, 1976; Tola, 1980; Savitz et. al., 1987) and more recently these reports include cancer of the mammary tissues (Kusano et. al., 1994; Azadniv et. al., 1995). Research leading to these recent report is still in the elementary stage and is therefore inconclusive. However, there are strong indications that with well planned and well executed research procedures, more definitive results may be forthcoming that will conclusively indicate that exposure to EMF play a role in the occurrence of breast cancer.

This research investigates this possibility since there is a surge in the number of women employed in occupations that expose them to EMF. With the advancement of technology as well as the increase in the development of new and more sophisticated household electrical appliances, many women are also at risk of exposure to EMF at home.

Cell-cell interaction play an important role in maintaining normal growth of normal cells. Cells make contact and communicate with each other via permanent structures such as gap junctions, lamellapodia, filopodia, and microvilli. However, immediately following cell divisions, daughter cells communicate with each other via cell surface receptors. The existence of these surface receptors has been shown to be responsible for the initial contact that occurs when fertilization is effected (Lopez et. al., 1985; Lopez and Shur, 1987; Cardullo and Wolf, 1995). GTase is a protein that acts as a receptor when located to the plasma membrane of cells. It has the affinity to bind the galactose on terminally galactosylated glycoproteins located on the plasma



membrane of other cells. The lock and key theory (Roseman, 1970) locates GTase on the key and terminally galactosylated glycoprotein in the lock. When the key fits into the lock by the binding of GTase to galactose, a temporary means of communication between daughter cells is established pending the formation of the structures that act as permanent means of communication.

However, these normal processes may be hindered when cells are exposed to cancer causing and/or cancer growth promoting agents. One hypothesis is that exposure to EMF promotes cancer formation or cancer growth rather than initiate it. Moreover, it has been established that EMF increases the rate of production of normal proteins as well as causes the syntheses of new proteins (Azadniv et. al.; 1994). This increase in syntheses especially at sites where the key and lock are located may prevent the key fitting perfectly into the lock. This type of increase has also been associated with increase in the incidences of plasma membrane projections in transformed cells (Brown and Browne, 1988) thus preventing the execution of the lock and key mechanism. Absence of fit will prevent the establishment of the temporary means of communication between daughter cells. The cells may then continue to divide nonstop causing tumors (Roseman, 1970; Pat and Grimes, 1974) which may become malignant. The cells may then proliferate thus spreading the cancer.

It has also been proposed that EMF can effect cytotoxicity by inhibiting the ability of T-lymphocytes to attack cancer cells (Severson et. al., 1988; Milham, 1988). EMF exposed cancer cells may also become more aggressive and demonstrate increased capacity to proliferate when compared to unexposed cancer cells.

If as previously suggested, that an increase in the syntheses of normal proteins may be cancer-causing, then an increase in the levels of ornithine decarboxylase activity may indicate malignancy. ODC plays a key role in the biosynthesis of polyamides, which are necessary for

protein and DNA syntheses and hence necessary for cell growth and differentiation. Its expression is very tightly controlled in all normal cells; however, regulation of its expression is altered in many tumor cells resulting in much higher levels of ODC in tumors. This increase in basal levels has been shown to play a causal role in the development of tumors by driving the continued proliferation and selective clonal expansion of initiated cells in epithelial tissues. Over-expression of ODC has also been shown to enhance tumor development in initiated keratinocyte cell lines (Murakami et. al, 1994; Clifford et. al., 1995; Megosh et. al., 1995). It may then be implied that agents such as EMF that may promote cell growth will increase ODC activity. An increase in the levels of ODC activity in cells exposed to EMF may then be used as an indicator of malignancy (Kusano et. al. 1994; Azadniv et. al., 1995; Kubota et. al., 1995).

This study is undertaken to show the effect that EMF exposure may have on the structural features of V12 cell line as well as any changes in ODC activity levels. The effect of EMF exposure on fibrocystic disease cells is also being studied in MCF-10 cell line.

The outcome of the study will determine the possibility of the development of invaluable tests, that may be used to screen women exposed to abnormal levels of EMF for the onset of breast cancer. This outcome may also be used to determine if the tumors in women suffering from fibrocystic disease, and exposed to abnormal levels of EMF have become cancerous.

## **MATERIALS AND METHODS**

**Cells:** Human female normal mammary V12 and fibrocystic disease mammary MCF-10 cell lines were kindly provided by Dr. Josiah Ochieng of Meharry Medical College. These cells are being cultured in DMEM containing epidermal growth factor, insulin, and cholera toxin (GIBCO Life Technology Laboratories, P.O. Box 68, Grand Island, NY 14072-0068), at 37°C under an atmosphere of 5% CO<sub>2</sub> in air. The cell stocks will be routinely subcultured by trypsinization with 0.25% trypsin: 1mM EDTA. The cells will be seeded into 75 cm<sup>2</sup> plastic tissue culture flasks (Corning 25110-75) for routine maintenance. The cells (at a density to be determined later) will be seeded in 100 mm petri dishes 24 hrs. prior to exposure to EMF. Five petri dishes per level of EMF exposure per time will be conducted. Four levels of EMF exposure and four exposure times will be investigated.

**Chemicals:** L-ornithine, benzethonium hydroxide, TPA, dithiothreitol, and pyridoxal-5-phosphate will be purchased from Sigma Chemical Co. (P.O. Box 14508, St. Louis, MO 63112). L-[1-<sup>14</sup>C] ornithine (50-60 mCi/mmol) will be obtained from New England Nuclear Research Products (Barley Mill Plaza, P-24, Wilmington, DE 19898).

**Electromagnetic Field:** A high power microwave oven will be used to generate different levels of EMF (20, 40, 60, and 80 Hz) that the cells will be exposed to. However, the cells will be maintained at 37°C even during exposure to EMF.

**Controls:** Both the V12 and MCF-10 cells will be exposed to TPA (0.1µg/mL) for periods similar to EMF exposure times as positive control treatments to confirm that treatment-related increases in ODC activity are detectable.

**Electron Microscopy:** Electron microscopic studies will be carried out on each cell line prior to

and after exposure to EMF to determine if any structural changes have occurred using previously established methods (George-Taylor et. al., manuscript in preparation).

**Cell Extracts:** Cell extracts will be prepared by removing growth medium from each culture dish at the end of EMF exposure and TPA treatment. The cell monolayers will be washed 3X with cold PBS. Cells will be removed and collected in 15mL centrifuge tubes (Corning 25311-15) and centrifuged for 5 min. at 2000 rpm. After decanting the PBS buffer, Tris-buffer (10mM Tris-HCl containing 1.72mM dithiothreitol pH 7.2) will be added to the cell pellet in cryogenic vials and kept in liquid nitrogen until assayed for ODC activity.

**Assay for ODC Activity:** ODC activity will be determined using L-[1-<sup>14</sup>C] ornithine as a substrate as previously described (Azadniv et. a., 1995).

**Assay for Protein:** The Lowry method will be used for protein determination (Lowry et. al., 1951).

**Date Analysis:** The ANOVA method will be used for data analysis, comparing ODC activity levels of EMF exposed cells to that of TPA treated control cells.

## **RESULTS**

The initial stage of the culturing of V12 and MCF-10 cells is proceeding as expected. Subsequent results will be made available as the different steps in the Methods are executed.

## **DISCUSSIONS**

No discussions of the results are available at this time.

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## **CONCLUSIONS**

No results and discussions that may be summarized are available at this time.

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## **ABBREVIATION**

ANOVA	-	Analysis of Variance
DMEM	-	Dulbecco Modified Eagles Medium
DNA	-	Deoxyribose nucleic acid
EDTA	-	Ethylene diamine tetra acetic acid
EMF	-	Electromagnetic Field
GTase	-	Galactosyltransferase
ODC	-	Ornithine decarboxylase
PBS	-	Phosphate buffered saline
TPA	-	12-O-Tetradecanoyl phorbol 13-acetate

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APPENDIX D1



# **DREW-MEHARRY-MOREHOUSE**

## **CONSORTIUM CANCER CENTER**

Charles R. Drew University of Medicine & Science

### **NATIONAL MAMMOGRAPHY DAY BREAST HEALTH SURVEY**

Survey #: \_\_\_\_\_  
Date: **OCTOBER 18, 1996**  
Location: Rodeo Rd & Crenshaw Blvd

**THANK YOU** for agreeing to fill out this survey. This survey asks questions about what you do to take care of your breasts. These questions are being asked of you so that you can help us design a women's breast health education program, specifically for women who live and work in this area of the city. It will take you about 10 minutes to answer all of the questions on this survey.

**This survey is anonymous.** Your name, address, and phone number should not be placed on any part of this survey.

**Most of the questions ask you to answer either "yes" or "no".** For some of the questions, you may need to write your answer. If you need some help at anytime during the survey, the staff person here will be happy to help you.

**You have the right to refuse to answer any of the questions you may feel uncomfortable answering.** If you don't want to answer any of the questions, you have the right to stop the survey; the staff person will take the survey back to the office and destroy it. Your decision to not do the survey will in no way affect any services or benefits you currently receive or for which you are applying.

**When you finish the survey, the staff person will give you \$5 in cash, and information for you to take home and read about taking care of your breasts.**

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1. WHAT IS YOUR DATE OF BIRTH:

\_\_\_\_\_ (Write your date of birth)

2. WHAT IS YOUR MARITAL STATUS ? : (Circle one answer)

- 01 MARRIED
- 02 SEPARATED
- 03 DIVORCED
- 04 SINGLE
- 05 LIVING WITH A PERSON OF THE OPPOSITE SEX
- 06 LIVING WITH A PERSON OF THE SAME SEX

3. WHAT IS YOUR RACE/ETHNICITY ? (Circle one answer)

- 01 AFRICAN AMERICAN/BLACK/NEGRO/COLORED
- 02 LATIN/HISPANIC
- 03 MEXICAN AMERICAN
- 04 ASIAN - PACIFIC ISLANDER
- 05 ASIAN AMERICAN
- 06 AMERICAN INDIAN
- 07 OTHER (SPECIFY): \_\_\_\_\_

4. HOW MANY CHILDREN DO YOU HAVE ?

\_\_\_\_\_ (Write the number of children)

5. WHAT IS THE HIGHEST GRADE OF SCHOOL YOU HAVE COMPLETED ?  
(Circle one answer)

- 01 6TH
- 02 7TH
- 03 8TH
- 04 9TH
- 05 10TH
- 06 11TH
- 07 12TH
- 08 SOME COLLEGE
- 09 BACHELOR'S DEGREE
- 10 MASTER'S DEGREE
- 11 DOCTORATE DEGREE

6. HOW OFTEN DO YOU ATTEND RELIGIOUS SERVICES?  
(Circle one answer)

- 00 Never
- 01 Every day
- 02 Two to three times a week
- 03 Once a week
- 04 Once a month
- 05 Five to six times per year
- 06 Only on special occasions

7. WHAT IS YOUR RELIGION ? (Circle one answer)

- 00 I DON'T HAVE ONE
- 01 CATHOLIC
- 02 EPISCOPALIAN
- 03 PRESBYTERIAN
- 04 MUSLIM
- 05 BUDDHIST
- 06 METHODIST
- 07 BAPTIST
- 06 OTHER (SPECIFY)\_\_\_\_\_

8. DO YOU WORK OUTSIDE OF THE HOME ?(Circle one answer)

- 00 NO
- 01 YES

9. NAME THREE THINGS THAT YOU WORRY ABOUT THE MOST. START  
WITH THE MOST IMPORTANT (Write your answers)

- 1. \_\_\_\_\_
- 2. \_\_\_\_\_
- 3. \_\_\_\_\_

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10. WHEN YOU THINK ABOUT YOUR HEALTH, NAME THREE THINGS THAT YOU WORRY ABOUT THE MOST. START WITH THE MOST IMPORTANT (Write your answers)

1. \_\_\_\_\_  
2. \_\_\_\_\_  
3. \_\_\_\_\_

11. WHO DO YOU USUALLY TALK TO WHEN YOU NEED INFORMATION ABOUT YOUR HEALTH,? (Circle all the answers that apply)

00 NO ONE  
01 MOTHER  
02 GRANDMOTHER  
03 AUNT  
04 DAUGHTER  
05 NIECE  
06 COUSIN  
07 FRIEND  
08 NEIGHBOR  
09 CO-WORKER  
10 MY DOCTOR  
11 A NURSE  
12 HUSBAND  
13 BOYFRIEND  
14 BROTHER  
15 UNCLE  
16 GRANDFATHER  
17 NEPHEW  
18 OTHER (SPECIFY): \_\_\_\_\_

12. DO YOU HAVE ONE DOCTOR WHOM YOU SEE WHEN YOU HAVE ANY PROBLEMS WITH YOUR HEALTH? (Circle one answer)

00 NO  
01 YES

13. HOW OFTEN DO YOU GO TO THE DOCTOR FOR REGULAR CHECK-UPS?

\_\_\_\_\_ (Write your answer)



14. DO YOU HAVE MEDICAL INSURANCE? (Circle one answer)

- 00 NO
- 01 YES

BREAST SELF-EXAMINATION OCCURS WHEN YOU EXAMINES YOUR OWN BREASTS WITH YOUR HANDS.

15. HAVE YOU EVER HEARD OF BREAST SELF-EXAMINATION?  
(Circle one answer)

- 00 NO
- 01 YES

16. HOW OFTEN DO YOU PERFORM BREAST SELF-EXAMINATION?  
(Circle one answer)

- 00 NEVER
- 01 DAILY
- 02 WEEKLY
- 03 MONTHLY
- 04 THREE-FOUR TIMES YEARLY
- 05 TWICE YEARLY
- 06 ONCE YEARLY

17. WHEN DO YOU THINK IS THE BEST TIME FOR A WOMAN TO PERFORM BREAST SELF- EXAMINATION? (Circle one answer)

- 00 NEVER
- 01 BEFORE MONTHLY PERIOD
- 02 DURING MONTHLY PERIOD
- 03 AFTER MONTHLY PERIOD

18. HAS ANYONE EVER TAUGHT YOU HOW TO DO BREAST SELF-EXAMINATION ? (Circle one answer)

- 00 NO
- 01 YES

19. HAS A DOCTOR/NURSE EVER SUGGESTED THAT YOU DO  
BREAST SELF-EXAMINATION? (Circle one answer)

00 NO  
01 YES

A CLINICAL BREAST EXAMINATION IS WHEN A DOCTOR OR NURSE  
EXAMINES YOUR BREASTS; THIS IS USUALLY DONE IN A MEDICAL  
OFFICE/ CLINIC.

20. HAVE YOU EVER HEARD OF CLINICAL BREAST EXAMINATION?  
(Circle one answer)

00 NO  
01 YES

21. HAVE YOU EVER HAD A BREAST EXAM DONE BY A DOCTOR OR  
NURSE? (Circle one answer)

00 NO  
01 YES

22. HAS A DOCTOR/NURSE EVER SUGGESTED THAT YOU HAVE A  
CLINICAL BREAST EXAM? (Circle one answer)

00 NO  
01 YES

23. HOW OFTEN DO YOU THINK A WOMEN SHOULD HAVE A BREAST  
EXAM DONE BY A DOCTOR/NURSE ? (Circle one answer)

00 NEVER  
01 DAILY  
02 WEEKLY  
03 MONTHLY  
04 THREE-FOUR TIMES YEARLY  
05 TWICE YEARLY  
06 ONCE YEARLY

**A MAMMOGRAM IS AN X-RAY OF THE BREAST TAKEN BY A MACHINE THAT PRESSES THE BREAST WHILE THE PICTURE IS TAKEN.**

**24. HAVE YOU EVER HEARD OF A MAMMOGRAM? (Circle one answer)**

00 NO  
01 YES

**25. HAVE YOU EVER HAD A MAMMOGRAM? (Circle one answer)**

00 NO  
01 YES

**26. IN THE LAST 5 YEARS HOW MANY MAMMOGRAMS HAVE YOU HAD?**

\_\_\_\_\_ (Write the number)

**27. WHAT WAS THE DATE OF YOUR LAST MAMMOGRAM ?**

\_\_\_\_\_ (Write the date)

28. HAS A DOCTOR/NURSE EVER SUGGESTED THAT YOU GET A MAMMOGRAM? (Circle one answer)

00 NO  
01 YES

24. IF YOU WERE ABLE TO RECEIVE A FREE MAMMOGRAM, WOULD YOU HAVE ONE DONE? (Circle one answer)

01 YES  
02 NO

FOR EACH STATEMENT BELOW, CIRCLE "01" IF YOU THINK THE STATEMENT A TRUE, OR "02" IF YOU THINK THE STATEMENT IS FALSE

	TRUE	FALSE
25. WHITE PEOPLE ARE MORE LIKELY THAN BLACKS TO GET CANCER	01	02
26. BLACK WOMEN ARE LESS LIKELY THAN WHITE WOMEN TO GET BREAST CANCER	01	02
27. BLACK WOMEN ARE MORE LIKELY THAN WHITE WOMEN TO DIE FROM BREAST CANCER	01	02
28. WOMEN CAN GET CANCER BY LETTING PEOPLE SQUEEZE THEIR BREASTS	01	02
29. HOW LIKELY DO YOU THINK IT IS THAT YOU WILL GET BREAST CANCER IN THE FUTURE? (Circle one answer)		

01 VERY LIKELY  
02 SOMEWHAT LIKELY  
03 SOMEWHAT UNLIKELY  
04 VERY UNLIKELY

FOR EACH STATEMENT BELOW, CIRCLE 01 IF YOU AGREE WITH THE STATEMENT AND 02 IF YOU DISAGREE WITH THE STATEMENT

- |     |   | AGREE | DISAGREE |
|-----|---|-------|----------|
| 30. | IF I HAVE BREAST CANCER, I WOULD RATHER NOT KNOW ABOUT IT   | 01    | 02       |
| 31. | CANCER IS A DEATH SENTENCE FOR MOST PEOPLE  | 01    | 02       |
| 32. | EVEN IF DETECTED EARLY, THERE IS NO CHANCE AT ALL OF CURING CANCER                                      | 01    | 02       |
| 33. | SURGERY CAN EXPOSE CANCER TO THE AIR AND CAUSE THE CANCER TO SPREAD                                     | 01    | 02       |
| 34. | I WOULD FEEL UNCOMFORTABLE LIVING WITH SOMEONE WHO HAS CANCER   | 01    | 02       |
| 35. | GETTING SCREENED FOR BREAST CANCER IS PROBABLY A GOOD THING TO DO                                       | 01    | 02       |
| 36. | HAS YOUR GRANDMOTHER/MOTHER/SISTER/DAUGHTER EVER BEEN DIAGNOSED WITH BREAST CANCER? (Circle one answer) |       |          |
|     | 00 NO   |       |          |
|     | 01 YES  |       |          |
| 37. | HAS ANY WOMAN IN YOUR FAMILY EVER DIED FROM BREAST CANCER? (Circle one answer)                          |       |          |
|     | 00 NO   |       |          |
|     | 01 YES  |       |          |
| 38. | HOW COMFORTABLE WOULD YOU FEEL TALKING WITH YOUR DOCTOR ABOUT BREAST CANCER ? (Circle one answer)       |       |          |
|     | 01 VERY COMFORTABLE   |       |          |
|     | 02 SOMEWHAT COMFORTABLE   |       |          |
|     | 03 SOMEWHAT UNCOMFORTABLE   |       |          |
|     | 04 VERY UNCOMFORTABLE   |       |          |

39. HOW COMFORTABLE WOULD YOU FEEL TALKING TO YOUR DOCTOR ABOUT MAMMOGRAPHY ? (Circle one answer)
- 01 VERY COMFORTABLE
  - 02 SOMEWHAT COMFORTABLE
  - 03 SOMEWHAT UNCOMFORTABLE
  - 04 VERY UNCOMFORTABLE
40. HOW COMFORTABLE WOULD YOU FEEL TALKING TO YOUR DOCTOR ABOUT CLINICAL BREAST EXAMINATION ? (Circle one answer)
- 01 VERY COMFORTABLE
  - 02 SOMEWHAT COMFORTABLE
  - 03 SOMEWHAT UNCOMFORTABLE
  - 04 VERY UNCOMFORTABLE
41. HOW COMFORTABLE WOULD YOU FEEL TALKING TO YOUR DOCTOR ABOUT BREAST SELF-EXAMINATION? (Circle one answer)
- 01 VERY COMFORTABLE
  - 02 SOMEWHAT COMFORTABLE
  - 03 SOMEWHAT UNCOMFORTABLE
  - 04 VERY UNCOMFORTABLE
42. HOW IMPORTANT DO YOU THINK IT IS TO YOUR FAMILY THAT YOU HAVE YOUR BREAST SCREENED FOR CANCER ON A REGULAR BASIS? (Circle one answer)
- 01 VERY IMPORTANT
  - 02 SOMEWHAT IMPORTANT
  - 03 SOMEWHAT UNIMPORTANT
  - 04 VERY UNIMPORTANT
43. HOW INTERESTED WOULD YOU BE IN RECEIVING INFORMATION IN THE MAIL ABOUT BREAST CANCER ? (Circle one answer)
- 01 VERY INTERESTED
  - 02 SOMEWHAT INTERESTED
  - 03 SOMEWHAT UNINTERESTED
  - 04 VERY UNINTERESTED

44. HOW INTERESTED WOULD YOU BE IN RECEIVING TRAINING ON BREAST SELF-EXAMINATION ? (Circle one answer)

- 01 VERY INTERESTED
- 02 SOMEWHAT INTERESTED
- 03 SOMEWHAT UNINTERESTED
- 04 VERY UNINTERESTED

45. IF A FREE BLOOD TEST WAS AVAILABLE THAT COULD TELL YOU IF YOU ARE AT RISK FOR DEVELOPING BREAST CANCER, WOULD YOU TAKE THE TEST? (Circle one answer)

- 00 NO
- 01 YES

45. IF THERE WAS RESEARCH THAT COULD TELL YOU WHETHER OR NOT A DRUG COULD PREVENT YOU FROM DEVELOPING BREAST CANCER, WOULD YOU PARTICIPATE IN THAT RESEARCH ? (Circle one answer)

- 00 NO
- 01 YES

46. WHAT IS YOUR ANNUAL INCOME? IS IT BETWEEN... (Circle one answer)

- 01 0-5,000
- 02 6-10,00
- 03 11-15,000
- 04 16-25,000
- 05 26-35,000
- 06 36-45,000
- 07 46,000 +
- 77 NOT SURE

47. DO YOU PLAN ON HAVING A FREE CLINICAL BREAST EXAM TODAY ? (Circle one answer)

- 00 NO
- 01 YES

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48. DO YOU PLAN ON HAVING A FREE MAMMOGRAM TODAY?  
(Circle one answer)

00 NO  
01 YES

THANK YOU FOR TAKING THE TIME TO ANSWER THESE QUESTIONS

REVISED 10/16/96

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APPENDIX D2

## **The Community Collective Breast Health Awareness Project (CCBHAP)**

### **AIMS**

Health Promotion Institute, Inc. (HPI), in collaboration with the Drew Cancer Center, Ujima Village Housing Community, and the Central and South Central units of the American Cancer Society, proposes to implement an intensive community-based breast health awareness and education intervention program. The overall goal of CCBHAP is to reduce the morbidity and mortality from cancer of the breast within a defined population of African American women in South Central Los Angeles. The specific aims of this intervention are to:

1. Increase the number of eligible African American women who access BCEDP providers for first-time mammogram, by a minimum of 30% above baseline levels;
2. Increase the number of eligible African American women who access BCEDP providers for repeat mammogram, by a minimum of 50% above baseline levels.
3. To increase the number of eligible African American women who access BCEDP providers for free CBE, by a minimum of 50% above baseline levels;
4. To increase the number of African American women practicing monthly breast self-examination (BSE), by a minimum of 25% above baseline levels;
5. Train a minimum of 5 African American female residents of a public housing community as Community Breast Health Change Agents.

These aims are consistent with the stated mission of Partnered for Progress to reduce breast cancer mortality in Los Angeles. Specifically, these aims are responsive to funding categories 1 and 5 of the Partnership mini grant. The aims will be achieved through the collective efforts of indigenous African American breast cancer survivors, community breast health change agents, and health professionals.

### **BACKGROUND**

Breast cancer is the most commonly diagnosed cancer among women in the United States.<sup>1</sup> One in eight women can be expected to develop invasive breast cancer during her lifetime.<sup>2</sup> In California, breast cancer accounts for nearly one in every three new invasive cancers diagnosed among women each year and one in every six cancer-related deaths among women. It is projected that in 1996, approximately 19,990 women in California will be diagnosed with invasive breast cancer, and 4,345 will die of the disease.<sup>1</sup> Nationwide, breast cancer is the leading cause of cancer death for African American women between the ages of 35-54 years.<sup>1</sup> Based on current breast cancer incidence rates, one in ten African American women in California will develop invasive breast cancer during her lifetime.<sup>3</sup> Breast cancer has been ranked first among the five most common cancer sites for African American women. When compared to white women, African Americans are at lower risk for developing breast cancer;<sup>1</sup> nevertheless, in California, the death rate due to breast cancer is 18% higher among African American women than their white counterparts. The importance of breast cancer prevention and early detection efforts targeted to African American women cannot be overstated. In spite of their lower incidence rate of breast cancer, African American women continue to suffer higher breast cancer mortality rates than either white or Latino women and lower 5-year relative survival rates.<sup>1</sup>

Breast cancer survival rates are worse for African American women than white women in all disease stages.<sup>4</sup> Current data inform that African American women experience a 5-year survival rate that is 10-15% lower than that of their white counterparts.<sup>1</sup> The disparity in breast cancer survival rates has been attributed to late-stage diagnosis of cancer, poverty, and limited access to quality care.<sup>4</sup> In California, African American women are at least 10% more likely than white women to be diagnosed with advanced stage, which contributes to their higher mortality rates.<sup>2</sup>

Routine breast cancer screening can diagnose cancers at an earlier stage, when the likelihood of survival is higher, and early diagnosis increases the likelihood of surviving breast cancer. Both ACS and NCI recommend palpatory breast screening by a physician or nurse and self-examination in conjunction with mammography to enhance early detection.<sup>1,5</sup> Despite medical and technological advances in early detection and treatment, under-utilization of breast cancer screening continues to be a challenge in many poor and African American women. Between 1987 and 1994, the percent of California women reporting a screening mammogram increased substantially, from 29% to 58%, respectively.<sup>6</sup> However, women reporting low income and low educational attainment are still screened less often. For example, as of March 1996, African Americans represent only 2.8% of the 13,864 women, statewide, who received BCEDP-funded screening mammograms. During the same period in Los Angeles County, African American women represent a mere 2.7% of the 7,535 women who received screening mammograms.<sup>7</sup> Reasons offered by many African American women for not seeking breast cancer screening include, being asymptomatic, the inability to afford health care, feeling embarrassed about someone/themselves touching their breasts, unwilling to interact with male physicians, and not having a family history of breast cancer.

Culturally competent, community outreach activities that address the cultural, structural, and personal breast cancer screening barriers for urban African American women are needed, if we are to impact upon the excessive breast cancer morbidity and mortality they suffer. Such programs should specifically address African American and lower-income women, who have low participation in cancer education and screening programs. The proposed intervention combines the strategies of role modeling, social support, and community mobilization to increase the number of African American women who access of BCEDP-funded screening mammograms and CBEs.

## **METHODOLOGY**

**Subjects.** The primary target population is African American female residents of a local public housing community who are (1) at least 40 years of age with no or inadequate insurance, or (2) younger than 35 years of age with a family history of breast cancer in a first degree relative. Latino female residents (3%) meeting these inclusion criteria are also eligible to participate.

**Site.** The Ujima Village Public Housing Community (Ujima) is located approximately six blocks west of the King-Drew Medical Center. The north, south, east and west boundaries of Ujima are 120th street, El Segundo Boulevard, Central Avenue, and Avalon Boulevard, respectively. The complex consists of 300 units, housing approximately 1000 residents on 10 acres of land. The most recent demographic data available (1995) indicates the ethnic profile of the residents is 97% African American and 3% Latino. Eighty percent of the residents are on AFDC and receive subsidized Section 8 housing. Most have no or inadequate health insurance. Approximately 25% (n=250) of the female residents are 40 years of age and older. The data on income, insurance status, and age suggest that a substantive number of the female residents meet the inclusion criteria for BCEDP. Based on previous outreach experiences with the Ujima community, an estimated 60% participation rate is expected (n=150).

**Design.** The intervention consists of six components: **Priming, Recruitment, Workshops, Follow-up, Training, and Evaluation.**

**Priming.** The Community Relations Director of Ujima Village, Merle Nobles, has agreed to serve as a Community Breast Health Change Agent. Ms. Nobles is a longtime resident of Ujima, and she has worked collaboratively on health and social service projects with the staff of HPI, Drew Cancer Center, and ACS. Ms. Nobles is respected and trusted by the Ujima residents. Along with the directors of housing and social services, she provides leadership and guidance for all social service-oriented programs occurring within Ujima.

Approximately one week preceding recruitment efforts, two priming activities will occur. First, the

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project director, a Special Touch Facilitator, will provide Ms. Nobles with a 1:1 training on the ACS Special Touch curriculum. Secondly, concurrent with training, Ms. Nobles will engage in a door-to-door mass communication effort to inform Ujima residents of the forthcoming breast awareness campaign. This latter activity will prime the residents for receptiveness to the intervention.

**Recruitment.** Packets of information on breast health, will be prepared for distribution to all adult female residents. The packets will contain informational/educational materials on breast cancer and breast cancer screening techniques (mammography, CBE, and BSE), a plastic shower card demonstrating BSE, the address and phone number for Watts Health Foundation (WHF; the local BCEDP provider), BSE and mammography promotional items (bookmarks, buttons, etc), and an invitation to attend an on-site breast health awareness workshop. During the first week of November 1996, from 9:00 am - 5:00 pm, Ms. Nobles and the project director will set up an information station in front of the administrative offices of the housing community. From this station, they will distribute the packets to all adult females who present to the administrative offices to pay their rent. Each woman who picks up a packet will be asked to complete a data sheet with her name, phone number, unit number, age/date of birth, and the relationship of any female relative diagnosed with breast cancer. The information of the women who meet the inclusion criteria will be transferred to a tracking log for follow up. All information collected will kept confidential. Data collected will be maintained in a locked file cabinet in the locked office of the project director, for which only the project director will have keys.

**Workshops.** All female residents will receive a written invitation to attend one of three breast health awareness breakfast workshops that will be convened, once monthly, between November 1996 and January 1997. The workshops will be held in the community room conveniently located on the grounds of Ujima, on Saturday mornings from 10:00 am to 12:00 noon. The proposed dates of the workshops are November 9, 1996, December 14, 1996, and January 11, 1997. Breakfasts will be prepared by senior residents of Ujima. The workshops will be co-facilitated by African American breast cancer survivors, a female physician/nurse practitioner, Ms. Nobles, and the project director. The WHF will be invited to pre-qualify and schedule screening appointments with eligible women, immediately following the workshop. At the beginning of each workshop, participants will be asked to complete a brief survey assessing their knowledge, attitudes, beliefs, and behaviors about breast cancer and breast cancer screening. With a format that is interactive, hands-on, supportive, and didactic, the aims of the workshops will be to: (1) increase the knowledge regarding the status of breast cancer in African American women; (2) provide a supportive space for women to dialogue with breast cancer survivors about their experiences with breast cancer screening, detection, and management; (3) emphasize the importance of routine screening for the early detection of breast cancer; (4) provide a culturally sensitive forum in which to address and negotiate barriers (personal, cultural, structural) to accessing mammograms; (5) exchange information about the existing BCEDP-funded breast cancer screening services available; (6) promote the use of the 1-800-4-CANCER number; (7) teach the correct technique for BSE; and (7) encourage the routine practice of BSE. Women may attend as many workshops as they desire.

**Follow-Up.** Breast cancer survivors of the same race and cultural background have been shown to encourage and empower other ethnically similar women to practice methods of breast cancer detection, by addressing existing attitudes, norms, and values regarding BSE and mammography.<sup>8</sup> The Central and South Central units of ACS have agreed to assist in the recruitment of African American breast cancer survivors to serve as the telephone interviewers for this project. Using pre-tested scripts and protocols, these interviewers will conduct three scheduled follow-up calls: (1) three days after the distribution of the information packets, (2) five days after the workshops, and (3) the within a week of their proposed CBE or mammography screening date. The purpose of these calls will be to encourage women to engage in some form of breast cancer screening behavior, and to ascertain whether or not eligible women are motivated at any point along the intervention to initiate screening behavior. For those women who access a screening mammogram, the follow-up calls will be

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used to encourage and monitor the women's compliance with mammography follow-up. An additional call (FUP4) will be made to women who do not report accessing some form of screening at previous calls or those who do not comply with mammography follow-up. A maximum of four calls will be made to each eligible woman. A schema of the follow-up is as follows: *Materials distribution-->FUP1-->Workshop-->FUP2-->Mammogram/CBE-->FUP3-->FUP4*. Participants will be supplied with a breast cancer screening form and a stamped enveloped addressed to the project office, and asked to mail their screening results to the project office. This process will dually accomplish the provision of the screening diagnosis and the verification of compliance with follow-up.

**Training.** Studies have shown that lay educators are effective in reaching low income African American females with breast cancer screening information. Women successfully completing all applicable components of the intervention before the January 14, 1997 workshop will be invited to become trained as Community Breast Health Change Agents. Along with Ms. Nobles, the project director will provide these women with 2,4-hour trainings covering breast cancer facts and figures, breast health and disease, frequency and proficiency of early detection tests, and BSE. Upon completing the training, participants will receive certificates of completion. All trainees will assist in the coordination and implementation of the January 14, 1997 workshop.

**Evaluation.** The project director will assume responsibility for the administration of the evaluation component. Both process and outcome evaluations will be completed. Data for these evaluations will be obtained from surveys (self-administered and telephone), activity and tracking logs, and sign-in sheets. A baseline survey will be administered at each workshop. A specific subset of items from the baseline survey will be used to gather information at each follow-up interview, to assess changes in breast cancer screening behaviors.

**Outcome Evaluation.** Stage at diagnosis will serve as the principal outcome measure. Other outcome measures will include the number of women reporting : (1) first-time mammogram (2) repeat mammogram (3) CBE, (3) BSE, (4)compliance with follow-up regimen. Another outcome measure will be the identification of the intervention component that effects a significant change in the number of women seeking screening mammogram, and the number of women who comply with mammography follow-up (see Scope of Work).

**Process Evaluation.** Process measures will focus on intermediate measures of intervention activities. These measures will evaluate the coordination and implementation of the materials distribution, recruitment and training of the breast cancer survivors as telephone interviewers, workshops, follow-up calls, incentive distribution, screening monitoring system, and the training of lay educators (see Scope of Work).

**INCENTIVES.** Participants will have three opportunities to receive incentives during this intervention. Incentives will awarded to women who: (1) attend the breast cancer workshop, (2) complete the survey, and (3) have a screening mammogram, return to the BCEDP provider for the results, and submit the results to the project office. Throughout the implementation of the intervention, the women will be reminded of the types of incentives offered for their participation. Each participant will be limited to receipt of one incentive per activity, on a one-time only basis. The proposed incentive schedule is as follows:

Activity	Incentive
Attend workshop	Gift certificate for holiday turkey (max value=\$10)
Complete survey	\$5.00 Cash
Screening mammogram + results	\$20.00 JC Penney gift certificate

Drew Cancer Center will encumber the costs of the five dollars (\$5) cash incentive for women completing the survey (see Budget). In addition to the incentives for the participants, Macy's gift certificates will be given to the telephone interviewers and the seniors who prepare breakfasts for the workshops. Drew Cancer Center will assist in the deferment of the costs associated with these incentives (see Budget).

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<p><b>B. Recruitment Activities</b></p> <ol style="list-style-type: none"> <li>1. Set up recruitment station             <ul style="list-style-type: none"> <li>- identify exact location for station</li> <li>- make arrangements for the delivery and set-up of tables and chairs for station</li> </ul> </li> <li>2. Place flyers announcing the distribution of materials at the counter where the women pay their rent</li> <li>3. Distribute info packets</li> <li>4. Have women complete data sheets</li> <li>5. Field questions and answers about the project and breast cancer</li> </ol>	<p>Proj Dir &amp; Ms. Nobles</p>	<p>10/28 10/28 10/28-11/8  11/1-11/8 11/1-11/8 11/1-11/8</p>	<p>Log of completed data sheets Log of eligible women</p>
<p><b>C. Workshops</b></p> <ol style="list-style-type: none"> <li>1. Reconfirm reservations for community room</li> <li>2. Identify at least 6 African American breast cancer survivors to co-facilitate workshops, and send letters of confirmation</li> <li>3. Identify at least 1 African American female nurse practitioner/physician to co-facilitate workshops, and send letters of confirmation</li> <li>4. Create invitations</li> <li>5. Create agendas</li> <li>6. Set up for workshops</li> <li>7. Conduct 3, 2-hour workshops, consisting of: breakfasts, administration of a baseline survey, overview of breast cancer among African American women, practicing BSE with MammoCare models, dialogue with breast cancer survivor, a review of BCEDP services, and prequalification of women for BCEDP services</li> <li>8. Distribute incentives to all women who complete the workshops</li> </ol>	<p>Ms. Nobles ACS, Proj Dir  ACS, Proj Dir  Ms, Nobles, Ujima resident Ms. Nobles, Proj Dir, breast cancer survivors, physician/nurse practitioner  Proj Dir, Ms. Nobles, Ujima residents  Ms. Nobles, Proj Dir, breast cancer survivors, physician/nurse practitioner, Watts Health Foundation  Ms. Nobles</p>	<p>10/15-10/31 10/15-11/1  10/15-11/1  10/28-11/8 10-28-11/8   11/9, 12/14 &amp; 01/11/97  11/9, 12/14 &amp; 01/11/97  11/9, 12/14 &amp; 01/11/97</p>	<p>Copies of workshop agenda  Rosters of presenters Copies of confirmation letters  Samples of invitation Copies of agendas   Sign-in sheets Survey findings  Incentive tracking log</p>

<p>D. Follow-up</p> <ol style="list-style-type: none"> <li>1. Develop 4 telephone scripts for fup calls</li> <li>2. Pilot phone scripts, and revise according to feedback</li> <li>3. Identify at least 6 African American breast cancer survivors to serve as telephone interviewers. These women will be recruited from the existing volunteer pool of ACS.</li> <li>4. Prepare training packets containing scripts, BCEDP info, and breast cancer Facts and figures</li> <li>5. Conduct a minimum of 3, 4-hour trainings with the telephone interviewers. Trainings will be held at the ACS offices from which the volunteers are recruited.</li> <li>6. Conduct a minimum of 3, maximum of 4 calls per eligible participant to assess: receipt of info packets, appointment status for CBE/mammogram, and compliance with mammography follow-up</li> <li>7. Distribute incentives to women who submit breast cancer screening reports</li> </ol>	<p>Proj Dir &amp; Ms. Nobles Drew Cancer Center ACS (Central/South Central)</p> <p>Proj Dir &amp; Ms. Nobles</p> <p>Proj Dir</p> <p>Telephone interviewers</p> <p>Ms, Nobles/ Proj Dir</p>	<p>10/20-11/5</p> <p>10/15-11/1</p> <p>10/20-10/28</p> <p>10/28-11/5</p> <p>11/12/96 - 01/25/97</p> <p>11/12/96 - 01/25/97</p>	<p>Copies of scripts</p> <p>Roster of telephone interviewers</p> <p>Copy of training packet</p> <p>Sign-in sheets</p> <p>Telephone follow-up log</p> <p>Incentive tracking log</p>
<p>E. Training of Community Breast Health Change Agents</p> <ol style="list-style-type: none"> <li>1. At the end of the first two workshops, extend invitations to residents to become trained as Community Breast Health Change Agents; recruit at least 5 women</li> <li>2. Identify convenient dates and times for training</li> <li>3. Conduct trainings, using a modified version of the ACS Special Touch curriculum</li> <li>4. The new Change Agents will co-facilitate the last workshop of the project</li> </ol>	<p>Proj Dir, Ms. Nobles</p> <p>Proj Dir, Ms. Nobles</p> <p>Proj Dir, Ms. Nobles</p>	<p>11/9, 12/14</p> <p>12/27/96 - 01/07/97</p>	<p>Roster of interested women</p> <p>Schedule of trainings</p> <p>Workshop agenda</p>



<p>F. Outcome Evaluation</p> <ol style="list-style-type: none"> <li>1. From baseline and follow-up surveys, determine the change in breast cancer screening behaviors.</li> <li>2. Determine the numbers of women who received first-time mammograms, repeat mammograms, CBE.</li> <li>3. Determine the number of women who practice BSE</li> <li>4. The number of women trained as Community Breast Health Change Agents.</li> </ol> <p>G. Process Evaluation</p> <ol style="list-style-type: none"> <li>1. Determine the mean number of follow-up calls made, the number of info packets distributed, the number of screening appointments made, the number of screening appointments missed, the number of workshops attended, the number of incentives distributed, the number of telephone interviewers recruited, the number of telephone interviewers trained, the number of presenters.</li> </ol>	<p>Proj Dir &amp; Drew Cancer Center</p> <p>Proj Dir &amp; Ms. Nobles Drew Cancer Center</p>	<p>11/9-01/31</p> <p>11/9-01/31</p>	<p>Completed surveys- baseline and follow-up Breast screening diagnosis form Follow-up surveys Sign-in sheets</p> <p>Follow-up tracking logs, sign-in sheets, data info sheets, incentive tracking logs, agenda, letters of conf</p>
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## APPENDIX E

## Estrogen Receptor Status of Breast Cancer: A Marker of Different Stages of Tumor or Different Entities of the Disease?

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Abstract — Breast cancer can be divided into two types according to the estrogen receptor (ER) level of the tumor, ER-positive and ER-negative. Two hypotheses have been raised about the relationship between ER-positive and ER-negative breast tumors. One hypothesis considers ER status as an indicator of a different stage of the disease. The other regards ER-positive and ER-negative tumors as different entities. For both etiological and biological studies of breast cancer it is important to know which hypothesis is correct. In this paper, we review evidence for and against each hypothesis and suggest issues to be addressed in future studies.

A substantial body of epidemiologic, experimental, and clinical evidence has shown that the effects of estrogens on the growth of breast epithelium influence breast cancer risk (1). Estrogens exert their effects by binding to estrogen receptors (ERs) in breast cells (2). Breast cancer has two subgroups according to ER status, ER-positive and ER-negative. Each subgroup has different biological and clinical attributes (3). Since estrogen stimulates cell proliferation of ER-positive breast cancer cell lines, and may therefore be associated with ER-positive human breast cancers only (2), an elucidation of the relationship between ER-positive and ER-negative cancers would have implications for etiologic studies of the disease.

#### TWO HYPOTHESES ABOUT ER STATUS

Two hypotheses have been raised about the relationship between ER-positive and ER-negative breast cancers (3, 4). One hypothesis suggests that ER status may represent different stages in the disease progress. This hypothesis stipulates that ER-negative breast cancers result from the lost ability to synthesize estrophilin during clonal evolution of estrogen receptors in ER-positive cancers (3,5). The other hypothesis considers ER-positive and ER-negative cancers as different entities. If the former hypothesis is correct, etiologic profiles of ER-positive and ER-negative tumors should be similar. If the latter hypothesis is true, the risk factor profiles may differ between the two types of breast cancer,

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especially for hormone-related factors such as nulliparity, age at first full-term pregnancy, age at menarche, and age at menopause.

### EVIDENCE FOR OR AGAINST EACH HYPOTHESIS

#### Comparisons of ER status according to tumor size and stage

If ER-negativity were associated with larger tumor size and/or later stage of breast cancer, it would support the linkage of estrogen receptor status with the stage of the disease. However, study results have been inconsistent. Some studies suggest that ER-negative status is related to late stage (6,7) or larger tumor size (7,8), while others suggest the opposite (9,10). More studies have actually failed to demonstrate an association between ER and stage or tumor size of the disease (11-18). White et al. (19) studied activated and non-activated ERs, and found that activated ERs are not associated with the stage of breast cancer. Using ER mRNA that is closely correlated with estradiol binding activity of ERs, Nagai et al. (20) also found that ER mRNA is not related to the clinical stage of the disease or tumor size. However, Pegoraro et al. (21) found that, in each racial group (white, black and Asian), very large tumors had fewer ERs, although the stage of the disease was not related to ER status.

These studies have been limited, because they were based on the comparisons in ER status of different patients with different tumor stage or size rather than the examinations of

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ER changes among the same patients. Many factors that might be associated with inter-individual differences may have confounded the results.

#### Comparisons of ER level according to tumor progression in the same patients

The most direct way to examine whether ER status is a marker of tumor progression is to follow-up patients' ER status as their tumors develop. Currently available data usually come from clinical studies. In these studies, ERs were compared between primary and recurrent or metastatic breast cancers from the same patients to examine whether ER level in primary tumors is predictive for that in recurrent or metastatic tumors. Because recurrent or subsequent cancers follow primary breast cancer, differences between primary and recurrent/metastatic tumors may represent a sequential change.

Simultaneously obtained specimens from primary and metastatic breast carcinoma have been compared for ER status (22-31). In general, primary and metastatic (mostly regional lymph nodes) cancers had a high ER status concordance - 85-93% (23,27,28,30). ER values from the primary and remote metastatic sites were also highly correlated (22,24,25,31), with the exception of one study (26). In patients whose ER status was discordant, changes in both directions (ER-positive to ER-negative and ER-negative to ER-positive) were observed (23,27,28,30). While Hoehn et al (22) showed that ER level

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tended to be higher in metastatic sites, Brankovic-Magic et al. (31) and Castagnetta et al. (29) found that receptor values were more likely to be lower in metastatic lesions.

ERs from sequential specimens of primary and recurrent/metastatic breast cancers without hormonal therapy have also been compared (23,24,27,28,30-35). ER status in sequential recurrent/metastatic tumors generally had a relative good agreement with that in primary cancers (23,24,27,28,32,35), although the magnitude of concordance (55-86%) tended to be lower than that for simultaneous specimens. ER levels were also correlated between the primary cancers and their recurrence or metastasis (30-32). The results discordance have shown both higher (27,28) and lower (30-32) ER levels in recurrent or metastatic lesions, and have also exhibited similar changes from positive to negative and from negative to positive (33,35). In another study comparing the primary tumor and bone metastases, ER levels were significantly lower in the bone metastatic lesions (34).

While temporal change might explain ER discordance between primary and metastatic lesions, other possibilities can not be excluded. Because ER-negative tumor cells are less differentiated and more aggressive (15,36,37), a selection of ER-negative cells during the development of metastases might produce lower ER levels in metastatic lesions (33). On the other hand, more ERs in metastatic lymph nodes may result from different histologic patterns. Higher cellularity in lymph nodes (31) and higher proportion of connective tissue stroma in primary tumors (25) may lead to more ERs found in metastatic



sites. However, cellularity may not entirely account for higher ER level in metastatic lesions, because changes from ER-positive status in primary tumors to ER-negative status in nodal metastases have also been found (30). The transition from ER-negative to ER-positive is inconsistent with the hypothesis of loss of ER as the disease progresses.

Comparisons of ERs in *in-situ* and invasive cancers from the same patients may be less subject to these potential problems. Kobayashi et al. (38) found that ER levels were higher for intraductal lesions and lower for invasive components in the same patients. However, another study, based on *in-situ* ductal breast carcinoma, showed that the proportion of ER-positive tumors was not higher than that in invasive carcinoma (29).

#### Studies of risk factors for breast cancer according to ER status

If ER status indicates different stages of a tumor, risk factor profiles should be same between ER-positive and ER-negative tumors. On the contrary, the risk factor profiles may differ if ER status represents two different entities of the disease.

Table 1 summarizes the epidemiological studies on selected risk factors according to ER status (40-46). The results have been relatively consistent for family history of breast cancer, history of benign breast diseases, and parity, and inconsistent for the other factors in the table and dietary factors (41,44,47). The risk associated with family history or benign

breast diseases tended to increase for both ER-positive and ER-negative tumors. However, increased risk for nulliparity was more likely seen for ER-positive cancers.

Four (41-44) out of six studies on the relationship between breast cancer and family history of the disease according to estrogen receptor status (41-46) demonstrated that relative risks of family history associated with breast cancer were similar for ER-positive and ER-negative tumors. However, two other studies found that family history is only related to ER-negative cancer (46) or has a stronger association with estrogen receptor-negative tumors (a relative risk of 5.7 for ER-negative tumors vs. 1.8 for ER-positive tumors) (45). Ideally, if ER status can be known from all affected family members, independent linkage analyses can be done to determine if the two ER status cancers have the same genetic mechanism(s). Unfortunately, only one study that we know of has considered this type of analysis (48). This study found that 5 out of 6 characterized patients were ER positive in one family, suggesting the needs of more studies.

Most studies have shown a tendency for women with benign breast disease to be at higher risk of developing both ER-positive and ER-negative breast cancers (41-43,45). However, with the exception of Kreiger et al.'s study (45), increased relative risk did not include unity for only ER-positive tumors (41,43) or ER-negative disease (42). In two other studies (40,44), the risk associated with benign breast disease tended to be lower for ER-negative cancers and higher for ER-positive tumors.

In six of seven studies (40-45), the tendency for nulliparous women to be more likely to develop breast cancer was shown only for estrogen receptor-positive cancers. This association appeared more obvious among premenopausal women in one study (41). However, almost all confidence intervals of the relative risks in these studies included unity.

Because of a relatively small number of epidemiological studies and possibly insufficient study power in some studies, evidence on the risk factor profile in terms of ER status has been inadequate. The aforementioned studies have not demonstrated consistent differences in etiologic factors between ER-positive and ER-negative tumors.

#### Genetic studies on the ER gene in relation to ER status

The expression of ER phenotype in tumor cells is controlled by the ER gene. There are two possible genetic changes for ER-negative tumors -- the loss of ER gene function and the suppression of ER gene expression. The former may result from structural rearrangements, chromosome losses, deletions and point mutations of the gene. The latter may be caused by inadequate activators for ER transcription, excessive transcriptional repressors, DNA methylation of the gene. Most studies have suggested the latter, showing that the human ER gene is not rearranged or deleted in ER-negative primary breast tumors (49,50) and that point mutations of the ER gene are also very rare in the tumors (51). Mechanisms of any of these genetic changes may be complex. If the changes occur with the

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progression of tumor, however, it suggests that ER-negative status, the lack of ER gene expression, may be associated with the progression of the disease.

However, studies of ER gene changes and their correspondence to tumor progression have been limited. One study (52) found that lower ER levels are associated with higher rate of rearranged chromosomes, an indicator of tumor evolution or progression. Studies that suggest the suppression of ER gene expression found that DNA methylation of the ER CpG island (cytosine-guanine dinucleotides) in the ER gene might be a mechanism for the suppression of the gene expression in ER-negative breast tumors (53,54). These results were confirmed by the reactivation of ER gene expression by demethylation of the ER gene (55). Suppression of the ER gene by methylation may occur during progression of the disease. In lung and colon cancer, it was found that hypermethylation on CpG island increases with progressive tumor stages (56,57) and may be related to increased DNA methyltransferase activity as the tumor progresses (58). If the suppression of the ER gene shares the similar mechanisms, that is, the suppression occurs during progression of breast cancer, ER-negative status may be an indicator of progressive breast cancer. Although not conclusive, these genetic studies suggest the possibility of the different-stage hypothesis.

In summary, previous studies have not provided the consistent evidence to conclude that either hypothesis is correct or even more plausible. Table 2 summarizes previous

studies according to study issue, the hypothesis supported if evidence is sufficient, and primary limitations. Excepting these limitations, the difficulties in follow-up of small tumors and biological complexity of ERs in terms of their expression, distribution and variation have further confined our ability to distinguish the two hypotheses.

### FUTURE STUDIES

Based on the above discussion, the following issues need to be addressed in future studies:

1. Follow-up of ER changes in tumors: Comparisons of ER status between primary and recurrent or metastatic tumors might not lead to an unique explanation of ER changes over time, as mentioned earlier. Sequential examinations of ER levels in a tumor are the best way to observe if ER status changes as the disease develops. While the difficulties may exist in obtaining sequential specimens of a tumor without interference of hormonal therapy, this type of study will provide the most direct evidence for or against the hypothesis of different stages.

2. Inclusion of small tumors: In most previous studies ERs were measured by using biochemical assays requiring substantial amounts of breast tissue (10,39). Therefore, small tumors, such as *in-situ* cancers, have often been excluded (59,60). However, ERs in the

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small lesions and their changes as the disease progresses to invasive lesion are very important for evaluating whether ER status represents the progress of breast cancer.

Immunohistochemical methods that have been recently developed (39) make it possible to measure ERs in small tumors.

3. Evaluation of effects of extraneous hormone: Due to the effect of hormone on ER levels (23,28), recent oral contraceptive (OC) use and estrogen replacement therapy (ERT) may decrease ER level, thereby resulting in the misclassification of ER status. For example, potential differences in risk factor profile between ER-positive and ER-negative tumors would be diluted in case-control studies because some ER-positive patients who have used OC or undergone ERT may be misclassified as ER-negative. In genetic studies, administration of estrogen has also been found to affect transcription and post-transcriptional modification of the ER gene (61). The possible effects should be avoided or evaluated in epidemiological studies and genetic studies in relation to the tumor progression.

4. Consideration of the possible effects of intratumor ER heterogeneity: The distribution of ERs is heterogeneous within a single tumor. On one hand, an ER-positive tumor can be falsely regarded as receptor-negative when an ER-negative area is sampled (10). The misclassification in ER status due to sampling errors can attenuate differences in risk factor profiles between ER-positive and ER-negative tumors in case-control studies.

The sampling errors in primary or/and metastatic lesions may influence comparisons of ER status between the two sites. On the other hand, the determination of ER status may depend upon not only ER content but also cellularity (59). For instance, ER-positive status may be defined for a highly cellular tumor consisting of cells of low ER content and ER-negative status may be assigned to a tumor with a very sparse distribution of ER-positive cells in a connective tissue stroma (59). Because of heterogeneity of ER distribution within a tumor and various cellularities between tumors, a more accurate definition of ER-positiveness and negativeness in terms of biological plausibility is desirable.

While efforts are needed to clarify which hypothesis is true, we do not exclude a third possibility: ER status of breast cancer represents neither different stages nor different entities --- ER-negative status may be a result of effects of various somatic and extraneous factors after tumor initiation that are not related to the tumor stage. Because ER status of breast cancer represents different survival length and response to hormonal therapy (2), it is desirable to know whether the two types of the tumor are two different entities and therefore have different biological and etiologic mechanisms.

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Table 1. Summary of case-control studies on breast cancer according to estrogen receptor status

Author (year)	ER status	Selected risk factors										Body size
		Family history	Parity	Benign breast disease	Age at first birth	Breast feeding	Age at menarche	Menopau- sal status	Age at meno- pause	Exogenous estrogen		
Hildreth, et al. (1983)	Positive Negative		- +	+* -	+ -	+ -				- +		
Hislop et al. (1986)	Positive Negative	+* +	- +	+* +	+ NA		- ±				± -*	
McTiernan et al. (1986)	Positive Negative	+ +	- ±	+ +*	+* ±	-* -	+ +*		+ +	+ -	+ +	
Stanford et al. (1987)	Positive Negative	+* +*	- ±	+* +	+ +	+ -		- -		- +	+ +*	
Cooper et al. (1989)	Positive Negative	+ +	- ±	+ -	+ +	NA -	NA -		+* +	- +	+ ±	
Kreiger et al. (1991)	Positive Negative	+* +*	- ±	+* +*	- -		- -	- -			± ±	
Yoo et al. (1993)	Positive Negative	- +	NA -		+ +	- -	+ +	+ NA				

+, positive association; -, negative association; \*, confidence interval(s) of OR(s) does not include one; NA, no association; ±, ORs are not proportional to the exposure levels.



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Table 2. Summary of previous studies according to study issue, hypothesis supported if evidence is sufficient, and study limitations.

Study issue	Hypothesis supported if evidence is sufficient	Primary limitations
Patients with larger tumors are more likely to be ER-negative	Different-stage hypothesis	Potential confounding by differences between patients with different stages.
Recurrent/metastatic lesions are more likely to be ER-negative than primary tumors	Different-stage hypothesis	Selectivity of ER-negative cells in metastatic sites; Different cellularity between primary and metastatic sites.
ER-positive and ER-negative tumors have different risk factor profiles	Different-entity hypothesis	Potential effects of hormonal products on ER status; Possibly insufficient study power.
The expression of the ER gene is suppressed with tumor progression	Different-stage hypothesis	Potential effects of hormonal products on the gene.

## **Methyl-Deficient Diets And Risk of Breast Cancer Among African-American Women: A Case-Control Study by Methylation Status of the ER Genes.**

Principal Investigator: Kangmin Zhu

Key Words: breast cancer; case-control studies; diet; estrogen receptors; methionine

Previous epidemiological studies using estrogen receptor (ER) levels as a measurement of ER status have obtained inconsistent results on whether ER-negative and ER-positive breast cancers have different risk factor profiles. Recent molecular studies show that ER-negative breast cancer results from the lack of ER gene transcription due to the methylation of the CpG island 5' to the gene. Because methyl-deficient diets can lead to abnormal DNA methylation and therefore carcinogenesis, we hypothesize that these diets are more likely to be associated with tumors with methylated ER genes. Interactions between the diets and other risk factors such as hormone-related risk factors may also differ according to the methylation status of the ER genes. The overall goal of this proposed study is to examine the relationship between methyl-deficient diet and breast cancer according to the methylation status of the ER genes among African-American women.

This study will use a case-control design. Female African-American patients ages 64 or younger who are diagnosed with breast cancer during 1995-1997 will be eligible as cases if they live in Davidson, Shelby or Hamilton Counties, Tennessee, and have household telephone services (n=497 approximately). The cases will be identified and selected through Tennessee Cancer Reporting System (TCRS). Controls will comprise African-American women without breast cancer who will be selected through random-digit telephone dialing, and frequency matched to cases according to age and residence area (n=497). Information on dietary methyl-components and other risk factors will be collected from telephone interviews. Information on ER status and tumor diagnosis will be obtained from medical records and TCRS files. Tissue specimens will be collected for the measurements of ER levels and the methylation status of the ER genes. Polytomous logistic regression method will be used to examine if the relationship between methyl-deficient diets and breast cancer risk differs by methylation status of the ER genes. The information from telephone interviews and medical records for 1995-96 cases and controls will come from a study that has been recommended to receive funding from Department of Defense.

Using the information we collect, we will be able to specifically examine:

- (1) Whether the methyl-deficient-diet/breast cancer relationship differs depending upon the methylation status of the ER genes in African-American women; and
- (2) Whether interactions between methyl-deficient-diets and other risk factors differ according to the methylation status of the ER genes of tumors.

## Proposal Relevance Statement

Previous studies of breast cancer risk factors according to estrogen receptor (ER) status of tumors have produced inconsistent results. This may be related to a number of factors. First, the mechanisms of causing ER variations are not well known. Therefore, hypotheses in previous studies were not sharpened based on the mechanisms. Second, the use of ER levels as an indicator of ER status is prone to the misclassification in the determination of ER status. For instance, a tumor with a sparse distribution of ER-positive cells may be falsely considered ER-negative.

We propose examining the association of methyl-deficient diets and breast cancer according to the methylation status of the ER genes in African-American women. This proposed study is innovative in two aspects. First, it combines the recent research progress on the ER gene with epidemiological investigations. The discovery of the effects of methylation on ER gene expression reveals the possible origins of ER variation, and makes it possible to establish an etiologic hypothesis based on the molecular characteristics. Second, the use of methylation status of the ER gene will overcome the drawbacks of ER levels as an indicator of ER status. Measurement of the methylation status of the ER gene is less likely to be affected by the cellularity of tissue specimens than determining ER status from ER levels. Therefore, by using methylation status, the misclassification will be reduced. Epidemiological studies using biomarkers have been increasing during the last decade, and represent a promising direction in etiologic research.

This study is relevant to the future prevention of breast cancer. First, any differences in the relationship between methyl-deficient diets and breast cancer may imply different etiologies between tumors with and without methylated ER genes. Because methyl-deficient diets are modifiable, knowledge from this study will eventually contribute to the prevention of the disease. Second, this study will target African-American women, a population that has never been studied for risk factors according to ER status of the disease. Because African-American women are more likely to develop ER-negative breast cancer that has a worse prognosis and is related to the methylated ER gene, a study in this population is of special importance.

## Background

Risk factor profiles of breast cancer may vary by estrogen receptor (ER) status of the disease because breast cell ERs may be important for the etiologic role of some risk factors such as estrogens. However, previous epidemiological studies addressing this have been inconsistent [1-9]. The inconsistency may be related to the use of total ER levels in defining ER status, and unclear mechanisms in ER variations.

Recent discoveries that ER-negative status results from methylation of the ER gene should help clarify the role of ER status on specific risk factors. First, the measurement of methylation status is unlikely to be affected by cellularity, thereby improving the determination of ER status. When ER levels are used, ER-positive status may be assigned to a highly cellular tumor with each cell having few ERs, and ER-negative status may be assigned to a tumor with few ER-positive cells [10]. Analysis of ER gene status should minimize this misclassification. Second, knowing the true patterns of ER gene expression may be important in assessing the impact of specific risk factors. Because methyl-deficient diets are related to abnormal DNA methylation, the diets may be a risk factor for tumors with the methylated ER gene, but not for those without. Based on these assumptions, we propose to explore the relationship between methyl-deficient diets and breast cancer risk according to methylation status of the ER gene.

The following paragraphs summarize the background information for this study:

- 1. ER gene methylation and ER status:** The human ER gene is located on chromosome 6q24-q27 [11,12]. Recent studies have shown that ER-negative breast cancer results from no ER gene transcription [11,13], and that this lack of expression is due to hypermethylation of the gene's 5' region [14]. This region was hypermethylated in 4 out of 5 ER-negative carcinomas and hypomethylated in 13 of 15 ER-positive carcinomas [13]. It has been further demonstrated that methylation of a cytosine and guanine rich area, termed a CpG island, in the 5' region and first exon of the gene is responsible for the lack of ER transcription in ER-negative tumors [15]. The impact of the CpG island methylation in ER-negative tumors was confirmed by the reactivation of the ER gene following demethylation [16].
- 2. Methyl-deficient diets, abnormal DNA methylation and cancer risk:** Studies show that diets low in methionine and folate or high in methyl group antagonists (such as alcohol) lower cellular levels of the methyl donor S-adenosylmethionine [17]. These changes cause abnormal DNA methylation patterns, such as global genomic hypomethylation and methylation of usually unmethylated CpG sites [18-20]. Therefore, diets reducing methyl-group availability can increase cancer risk in both animal models [21] and humans [22,23], probably as a result of these DNA changes. For example, a combination of high alcohol and low methionine and folate intake conferred a relative risk of 7.4 for distal colon cancer [23].
- 3. Methyl-deficient diets, methylation status of the ER gene and breast cancer:** Because methylation of usually unmethylated CpG sites is associated with low dietary methyl-components, tumors with the methylated ER gene may be especially susceptible to the effects of methyl-deficient diets and methyl-antagonists. On the other hand, these dietary factors may be less influential and other risk factors may be important for tumors without the methylation. A recent study in which alcohol, a methyl-antagonist, appears to be associated only with ER-negative breast cancers suggests this possibility [8].

## Hypothesis/Purpose

We hypothesize that methyl-deficient diets cause the abnormal gene methylation and therefore relate to the carcinogenesis of breast cancer with the methylated ER gene only. We further hypothesize that hormone-diet interactions differ between tumors with and without the methylation because of differential expressions of ERs.

African-American women are a population that has never been studied according to ER status, although they are more likely to develop ER-negative breast cancers (presumably with methylated ER genes) that have a worse prognosis. The overall goal of this proposed project is to evaluate the effects of methyl-deficient diets and methyl-antagonists on breast cancers with and without the methylation of the ER gene among African-American women.

## Technical Objectives

A case-control study is proposed and will specifically aim to: (1) examine whether the relationship between methyl-deficient diets/methyl-antagonist intake and breast cancer differs between tumors with methylated and unmethylated ER genes, and (2) evaluate whether there are different interactions between these dietary factors and hormone-related risk factors, depending upon the methylation status of the ER gene. Additionally, we will analyze correlations between ER levels and the methylation status of the ER gene, and factors that may be related to the correlations.

## Methods

### 1. Study subjects:

A case-control design is proposed for this study. Cases will primarily come from an exploratory case-control study that has been recommended to receive support from the Department of Defense (UIS#'s RP951646). This original exploratory study aims to examine breast cancer risk factors according to ER status extracted from medical records. Cases in the study consist of female African-American patients ages 64 or younger diagnosed with breast cancer in Davidson, Shelby and Hamilton Counties, Tennessee, between 1995 and 1996. In order to increase the study power, we will enroll additional cases diagnosed in the three counties in 1997 for this proposed study.

The cases with breast cancer will be selected through the Tennessee Cancer Reporting System (TCRS). By law, all hospitals and certain laboratories are required to submit specific cancer data about patients they diagnose within six months to the Tennessee Department of Health. These data include information about the patient's identification, demographic characteristics, and tumor diagnosis. All breast cancers (ICD-O site code C50) [24] will be histologically confirmed.

According to data from TCRS, there were 357 African-American women aged 64 and younger diagnosed with breast cancer in Davidson, Shelby and Hamilton counties in 1991 and 1992. During the 3-year period of the proposed study, an estimated number of 536 African-American breast cancer patients will occur in these counties. In this study, only patients who have a telephone will be eligible since we are using controls selected through random digit dialing. According to statistics in 1994 [25], the percent of African-American households with telephones was 85%, 91% and 90% for age groups of 25-54, 55-59 and 60-64, respectively. Based on these values, we will have 497 cases. Assuming that 5% of the cases have died or moved by the onset of the study, 95% of physicians will give permission to contact their patients, and 85% of patients with doctor's permission will accept an interview, we expect 381 subjects to participate in the study. We further assume that tumor tissues will not be available for 5% of participants; therefore the final number of cases in the study will be about 362.

Controls will consist of African-American women without a history of breast cancer. The controls will be selected using random digit dialing techniques, and frequency matched to the corresponding cases on 5-year age range and residence area. The area of residence will be defined by telephone exchange.

The first step of control selection by random digit dialing (RDD) will be to group cases whose telephone area codes and prefixes serve the same area. Then, the sampling frame by age distribution of the cases in the area will be formed. By randomly selecting one of the telephone prefixes of the cases and adding four randomly-selected digits, a call will be made to find an eligible woman. We will use an eligibility table to recruit controls into age strata in the appropriate proportion needed for the study evenly over the entire period of the study, applying the one-step method (method B) developed by Hartlow and Davis [26].

Numbers that are not answered will be called up to 9 times over a two-week period, including 3 day-time, 3 evening and 3 weekend calls. For each telephone number, interviewers will determine (1) whether it is residential or non-residential; (2) whether there are any eligible women at a residential number; (3) how many eligible women there are (randomly select one using the last two digits of the telephone number, if more than one eligible woman); and (4) whether an eligible woman consents to have an interview. We will improve the efficiency and response of RDD calls by obtaining counts of business and residential accounts according to each working prefix from local telephone companies and avoiding all prefixes that have only business and no residential numbers. All call outcomes will be recorded. The Department of Family and Preventive Medicine,

Meharry Medical College, has a computerized telephone interview system. Using this system and the random digit dialing technique, the department has conducted a number of population-based surveys among African-Americans and accumulated vast experience with the RDD technique in the proposed study areas.

In order to optimize the proportion of patients who agree to participate, a monetary incentive of \$35 will be provided. We will also provide participants a chance to win \$150 by random drawing each year.

## 2. Data collection

After a patient is reported to TCRS, her eligibility in terms of primary tumor site and age at diagnosis will be assessed. The name, address and telephone number of an eligible patient's physician will be obtained, and a letter and a consent form will be mailed to the physician. This letter will describe the study and request the physician's permission to contact the patient. We will also request the patient's telephone number. If a physician does not return the consent form, one of our staff members will call the physician's office to determine the status of the letter and request a response. Once we obtain a doctor's consent, a cover letter and a consent form will be subsequently mailed to the potential subjects to schedule an interview. In the letter and consent form, the study procedures and a subject's right as a research participant will be stated. Subjects will be asked to sign and return the consent form in an enclosed stamped envelope.

For controls who are selected by RDD and are eligible for the study, we will describe the study purposes and procedures on the phone, mention monetary incentives, and ask whether they will agree to a telephone interview. Telephone interviewers, who will be well trained in telephone interviewing skills, general knowledge of breast cancer, and ways to address the concerns of a subject, will answer questions about the study. For those who agree to participate in the study, a telephone interview will be made or scheduled.

We will use the following protocols:

(1). Telephone interview: Detailed procedures and the questionnaire for telephone interviews have been provided in the original proposal and its technical revision. Briefly, questions on potential risk factors at or before the reference date (the date of diagnosis for cases and the corresponding date for controls) will be asked during the interview, including (a) demographic variables, (b) reproductive factors and menstrual status, (c) medical history, (d) family history of cancer, (e) personal habits (smoking and alcohol consumption) and medication use, (f) anthropometric measures, (g) environmental risk factors, (h) screening for breast cancer and medical care use, (i) detection mode and treatment of breast cancer (for cases only). Dietary intakes will be estimated using the Block-NCI Health Habits and History Questionnaire [27]. Dietary methyl-content is defined by methionine and folate intakes. Methionine, folate and other nutritional intakes will be computed using composition values from U.S. Department of Agriculture sources [28] and other supplemental data.

(2). Laboratory tests: For a subject who gives consent to use tumor tissue, her tumor tissue will be obtained from the pathology department where the diagnosis was made. The procedures for handling tumor tissues will follow the detailed guidelines. Immediately after tissue specimens are obtained, they will be stored at ultra-low temperatures on dry ice, and shipped to Meharry Medical College. These specimens will be stored at -80°C until use and will be used for the measurement of steroid receptor levels and methylation of the ER genes. All laboratory work will be guided under the quality control procedures.

The methylation status of the ER CpG island will be measured using Southern blot analysis of DNA digested with restriction enzymes sensitive to DNA methylation [15]. If a CpG island is unmethylated, *NotI*-*EcoRI* double digests will produce two bands - 1.2 and 1.9kb in length when probed with a 3.1 *EcoRI* fragment at the 5' end of the gene. If the ER CpG island is methylated, *NotI* will not digest the fragment and a 3.1kb fragment will be detected. Other methylation sensitive enzymes will be used to confirm the methylation pattern [15].

ER analysis will be carried out with an ER immunohistochemical analysis (ER-ICA) kit (Abbott Laboratories, North Chicago, IL) [29,30]. ER-positive is defined as 5% or more neoplastic cell nuclei showing staining [29]. This analytical method is chosen because it is rapid, less tissue is needed, and it is highly correlated with the biochemical assay results that may be used in some hospitals [30].

(3). Tennessee Cancer Reporting System files: We will obtain information about the diagnosis of breast cancer from computerized files of the Tennessee Cancer Reporting System. The information will include date of

diagnosis, primary site, histology, grade or differentiation, diagnostic confirmation approach, SEER Stage, AJCC stage, and treatment.

(4). Medical records of cases will be reviewed for estrogen receptor status (positive or negative), estrogen receptor assay values, hospital where a measurement was made, measurement method and hormonal use before ER measurement and pathological diagnosis. A trained medical record abstractor will perform all extractions, using a standardized data collection form and a medical record review manual.

### 3. Data processing

A subject tracking system will be developed to integrate data from the different sources. The data files created for the tracking system will consist of (1) the physician file, (2) TCRS file, (3) the subject file including questionnaire data, and (4) medical record and laboratory test file. These four files will be linked together to retrieve up-to-date information about the status of the study.

An editing will be taken shortly after the interview with a subject. During editing, a completed form will be examined for any errors, inconsistency, unusual answers and missing values. Corrections or compensations will be made by calling back the subject when possible. After data are entered on the computer, another round of checks will be conducted to correct any errors in data entry.

### 4. Data analysis

(1). Comparability of cases and controls: The distribution of demographic variables and risk factors will be illustrated in terms of case-control status and the methylation status of the ER genes. Chi-square analysis will be used to test for homogeneity [31].

(2). Association of methyl-deficient diets with breast cancer: Polytomous logistic regression will be used to evaluate the relationship between breast cancer and methyl-deficient diets/alcohol consumption according to the methylation status of the ER gene [32,33]. In this analysis, three groups will be compared, cases with methylated ER gene, cases with unmethylated ER gene and controls. In contrast with pairwise logistic regressions by ER status, polytomous logistic regression has the following advantages: (1) slight improvement in estimator precision, (2) a simultaneous test of whether odds ratios (ORs) from two case-control comparisons are both one, and (3) test of homogeneity of ORs from two case-control comparisons even if confounders are different for the two comparisons. Interactions between methyl-deficient diets/alcohol consumption and other risk factors such as hormone-related factors will also be evaluated in terms of the methylation status of the ER gene.

In the analysis, we will address potential problems due to the correlation of methionine and folate intake with other nutritional components (such as multivitamine use and protein). First, we will define a methyl-group intake variable by combining methionine, folate and alcohol intakes (this synthetic variable is less likely to be correlated with any other single nutritional component). Second, nutritional components that may be potential confounders will be adjusted in logistic models. Another issue that we will consider is that association between methyl-deficient diets and breast cancer without the methylation may result from the effects of the diets on tumor progression if the methylation of the ER gene is an indicator of disease progression. To assess this possibility, we will analyze data by tumor stage and methylation status. If the ER gene methylation status of the gene is only related to the progression of the disease, then the OR estimates will be higher for late-stage tumors. The last consideration is the potential effects of hormonal use prior to tissue collection on methylation status. We will exclude the cases with pre-diagnostic hormonal use from analyses, to assess this confounding possibility.

(3) Correlations between ER levels and the methylation status of the ER gene: Using data from cases, we will use kappa index or correlation coefficient to assess correlation [34,35]. The analyses will be done in terms of tumor tissue source, pathologic characteristics and demographic variables of cases to evaluate factors that may affect the correlation level. We expect that information from the analyses will help define a new pathway to ER status.

### 5. Sample size and study power

Assuming that the overall proportion of methylated ER genes is similar to that of ER-negative status among African-American patients (42%) [36], we will have 152 and 210 cases with methylated and unmethylated ER genes. An equal number (n=362) of controls will be selected.

Our primary study aims are to investigate the relationship between methyl-deficient diets/alcohol intake and breast cancer risk according to ER gene methylation. Because there are no power estimation methods available for polytomous logistic regression analysis, it is impossible to generate such estimates. Instead, applying pairwise logistic regression method, we have estimated the power estimates for the methylation subgroup (we assume no increased risk of the diets for tumors without the methylation).

Information on relative risk and the distribution of risk factors among controls is necessary for the estimation of study power. Because no such studies by the methylation status of the ER genes have been done for breast cancer, any power estimates based on assumed ORs are speculative. Instead, we estimated minimum detectable odds ratio at the power of 80%, using the distribution of dietary folate and methionine and alcohol intake in controls from previous studies [23,37,38]. Table 1 shows the minimum detectable odds ratios for methyl-deficient diets and alcohol for tumors with methylated ER gene. One-sided type I errors were used in the estimations, because previous studies on breast cancer have seldom shown an OR lower than one for alcohol consumption and higher than one for diets rich in methionine and folate.

Power estimates to assess interactions between risk factors are not calculated. A recent study on genotype-environmental interactions suggests that inclusion of interactions can actually improve the study power of the original study without considering interactions [39]. Therefore, consideration of interactions in this study may not decrease the study power.

## 6. Strengths and limitations

This is the first study to test the hypothesis using both epidemiological and molecular biological methodology. Since information on risk factors will come from a project that will be supported by Department of Defense (DOD) for most study subjects, it is possible to conduct such a population-based study with a limited budget for this award category. The proposed study will recruit more cases and controls and measure ER status using standardized laboratory procedures. Because this information may also be available for the original study that has been recommended for support from DOD, the original study will also be strengthened due to more reliable ER information and increased study power.

The determination of ER status may depend not only upon ER content but also cellularity [10] and therefore, a tumor with a sparse distribution of ER-positive cells may be falsely considered ER-negative. The methylation status of the ER genes, which is less prone to this problem, may be a better indicator of ER status.

Non-participation of eligible women in the study is a potential problem. We expect that monetary incentives will minimize this problem. Furthermore, we will evaluate the potential effects of non-participation using demographic and pathological data from TCRS, and adjust for the bias with appropriate statistical methods [40].

Missing data due to unavailable tissues may be another problem. However, the inability to obtain samples may not be associated with either methyl-deficient diets or the methylation status of the ER gene and therefore may not substantially bias the results. Nevertheless, we will evaluate any potential effects, using data from TCRS, medical record reviews and telephone interviews.

## Award Category Special Requirements

This proposed study is consistent with the theme of innovation for the IDEA subcategory (please refer to Proposal Relevance Statement).

## Investigator's Qualifications

Dr. Zhu, the Principal Investigator, has ever been involved in several cancer epidemiological studies and is qualified to conduct the proposed study.



Table 1. Minimum detectable odds ratio at the power of 80% for tumors with methylated ER gene

Variable	Proportion of exposure in controls (%)	Minimum detectable odds ratio
Folate (ug/day)		
>282	25	1.8
<=282	75	
Methionine (g/day)		
>2.96	25	1.8
<=2.96	75	
Alcohol		
Never use	35	1.7
Ever use	65	
No-alcohol-high methionine/folate		
Yes	12	2.4
No	88	

## Abstract

Using data from Medicare (1992-1993) and the Tennessee Cancer Reporting System (1992), we compared African-American and white women, aged 65 and older, within and outside the Mississippi Delta region of Tennessee, on the use of mammography and stage of breast cancer at first diagnosis. The Mississippi Delta region is economically poorest in the U.S. Our results showed that while African-American women were less likely to have had a mammogram than white women in non-Delta areas (25.6% vs. 30.6%, OR=0.77, 95% confidence interval (CI) 0.74-0.80), the corresponding difference was greater in Delta areas (16.1% vs. 31.9%, OR=0.41, 95% CI 0.39-0.43). The proportions of early breast cancer in African-American women were lower, compared with those in white women, in both Delta and non-Delta areas. The results suggest that mammography might be least used in older African-American women in economically poor areas and future intervention programs on breast screening should target the minority communities with the greatest need.

The effectiveness of breast cancer screening on decreasing mortality of the disease among women aged 50 years and over has been well demonstrated [1,2]. It is estimated that deaths of breast cancer would be decreased by 25% to 30% if screening mammography could be universally used [3]. However, regular breast screening is underused among older women [4,5]. Data showed that the proportions of women who ever had a mammogram were decreased with increasing age [4,6]. The lower use of the screening is also pronounced among African-American women [7,8] or indigent women [9]. African-American [10] and poor [9] women are less likely to undergo breast screening, as compared with their white or richer counterparts [10]. Because of the lower use of mammography, breast cancer is more likely to be diagnosed at later stage in these populations.

Because of the reported relationship between decreased mammography use, poverty and African-American ethnicity, we hypothesized that less use of mammography is most serious among African-American women in the poorer areas of Tennessee. Stage of the disease at diagnosis may also be latest in these women in the areas, because stage of breast cancer is related to the use of breast screening. Using data from the U.S. Department of Health and Human Services and Tennessee Cancer Reporting System (TCRS), this study compared race-specific mammography rates in older women between Tennessee counties in the Mississippi Delta region (poverty areas) and those non-Delta counties (non-poverty areas) to identify the population that is least likely to use mammography.

## MATERIALS AND METHODS

### **Study design and data sources:**

This study used a cross-sectional design. Study areas included all counties in Tennessee. We classified counties into those Delta and non-Delta counties using

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definitions of the lower Mississippi Delta Deveopment Commission [11]. Delta region is economically poorest in the U.S.

Using data from the "1992-93 Mammography Services Paid by Medicare" by the U.S. Department of Health and Human Services [12], we collected information on mammography use among women aged 65 and over. The Medicare program enrolls about 96% of women aged 65 and over [13]. Since January 1991, Medicare has begun a biennial screening mammography program and reimburses 80% of cost for the procedure. Therefore, data from Medicare since 1991 can reasonably be used to reflect the mammography use in the general female population aged 65 and older during the period.

We collected information on breast cancer stage at diagnosis from registry data of the Tennessee Cancer Reporting System (TCRS) in 1992. TCRS was established in 1986. According to the Tennessee legislature, all hospitals and certain laboratories are required to submit to the Tennessee Department of Health and Environment specific cancer data about patients they diagnose. Thus, TCRS data include almost all cancer patients diagnosed in the state. The data reported to TCRS contain information about patient's demographic characteristics and tumor characteristics such as stage. The in-situ and localized tumors according to the classification of Survellance, Epidemiology, and End Results were defined as early-stage breast cancer.

### **Data analysis**

We compared the mammography rates between two racial groups (African-Americans vs. whites) according to area (Delta and non-Delta counties). For two comparision groups, we calculated odds ratio (OR) estimates and their 95% confidence intervals (CI) [14]. Black/white differences tend to be greater in poverty areas if race and poverty have synergetic effect on the use of mammography.

We also compared the proportions of early-stage breast cancer according to area and race. Early-stage tumors were defined as those with stage A and B. Odds

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ratio (OR) estimates comparing tumor stages between African-American and white women and their 95% confidence intervals (CI) were calculated according to Delta or non-Delta counties.

## RESULTS

Table 1 shows the mammography rates among older African-American and white women in the non-Delta counties. While 31 percent of white women have ever had a mammogram during 1992-1993, only 25 percent of African-American women have ever undergone such a procedure. The odds ratio estimate was 0.77 (95 percent CI 0.74-0.80). The black/white difference became greater in the Delta counties, where only 16 percent of African-American women had a mammogram during the two year period while the proportion in white women was similar (table 2). The odds ratio estimate decreased to 0.41 (95%CI 0.39-0.43).

The result on the stage of breast cancer at diagnosis in the non-Delta counties was presented in table 3. While 73 percent of white women had breast cancer diagnosed at an early stage, the corresponding proportion was only 55% for African-American women (OR=0.46, 95%CI 0.27-0.78). A similar black/white difference was found in the Delta counties (table 4).

## DISCUSSION

The study results showed that there were substantial differences in the mammography use and the stage of the disease between African-American and white women, and between areas with different economic level. The problem of the underusing mammography was more serious among elderly African-American women in poverty areas because of possible synergism between poverty and African-American background. We predict that, similar to that in the mammography use, the difference in the stage of breast cancer between African-American and white women is greater in the Delta counties. However, a similar black/white difference

was found in the proportion of early stage breast cancer between Delta and non-Delta areas. One of the potential explanations of this inconsistency between the mammography use and stage of the disease might be the difference in time frame. Only 1992 data was available from TCRS when this study was conducted, although 1992-1993 Medicare data were used. While one-year cancer data contained less patients (especially African-Americans) and therefore were subject to a greater sampling error, a high consistency might not be achieved due to the fact that two datasets did not cover the same period.

The Year 2000 goal is to provide breast screening to 80% of all women over the age of 40 years [15]. To meet the goal, it is imperative to increase breast screening among older women because of their high mortality of the disease and low rates of having breast screening [8]. In Tennessee, a number of mammography screening and intervention programs are being performed. However, because of limited resources, targeting priority populations is important for using the resources efficiently. The results of this study are significant for policy-makers in resource allocation to improve the use of breast screening in the state. To use the resources efficiently for increasing mammography use in Tennessee, more attention should be taken to the population with the greatest needs, older African-American women in economically poorer areas.

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Table 1. Mammography usage in African-American and White women aged 65 and older in Tennessee counties of the non-Delta region, 1992-1993

	Mammogram		
	Yes	No	OR (95%CI)
White	61666 (30.6%)	139975 (69.4%)	1.00(Reference)
Black	3905 (25.3%)	11560 (74.7%)	0.77 (0.74-0.80)

Table 2. Mammography usage in African-American and White women aged 65 and older in Tennessee counties of the Delta region, 1992-1993

	Mammogram		
	Yes	No	OR (95%CI)
White	21116(31.9%)	44979 (68.1%)	1.00(Reference)
Black	3329(16.1%)	17294 (83.9%)	0.41 (0.39-0.43)

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Table 3. Stage of breast cancer at diagnosis in African-American and White women aged 65 and older in Tennessee counties of the non-Delta region, 1992

	Stage of breast cancer		
	Early	Non-early	OR (95%CI)
White	668 (73.0%)	247 (27.0%)	1.00 (Reference)
Black	37 (55.2%)	30 (44.8%)	0.46 (0.27-0.78)

Table 4. Stage of breast cancer at diagnosis in African-American and White women aged 65 and older in Tennessee counties of the Delta region, 1992

	Stage of breast cancer		
	Early	Non-early	OR (95%CI)
White	222 (73.0%)	82 (27.0%)	1.00 (Reference)
Black	35 (54.7%)	29 (45.3%)	0.45 (0.25-0.80)

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DEPARTMENT OF THE ARMY  
US ARMY MEDICAL RESEARCH AND MATERIEL COMMAND  
504 SCOTT STREET  
FORT DETRICK, MARYLAND 21702-5012

REPLY TO  
ATTENTION OF:

MCMR-RMI-S (70-1y)

1 JUN 2001

MEMORANDUM FOR Administrator, Defense Technical Information  
Center (DTIC-OCA), 8725 John J. Kingman Road, Fort Belvoir,  
VA 22060-6218

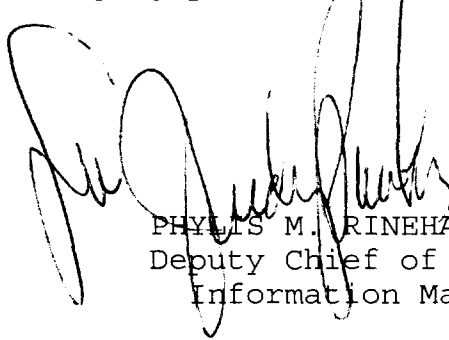
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2. Point of contact for this request is Ms. Judy Pawlus at DSN 343-7322 or by e-mail at judy.pawlus@det.amedd.army.mil.

FOR THE COMMANDER:

Encl

  
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